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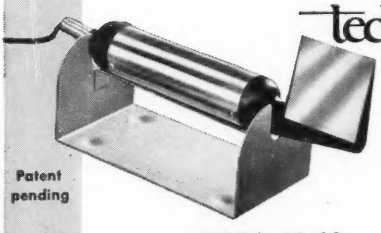

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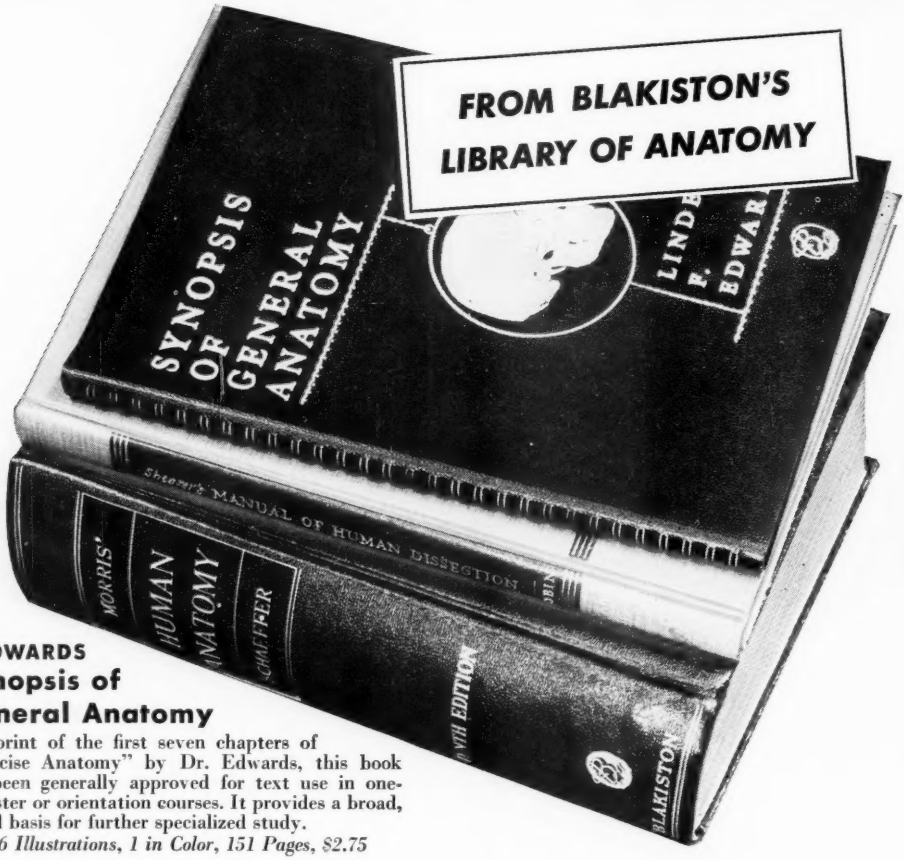

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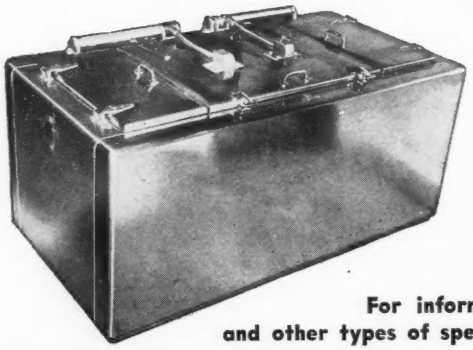

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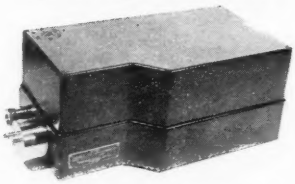

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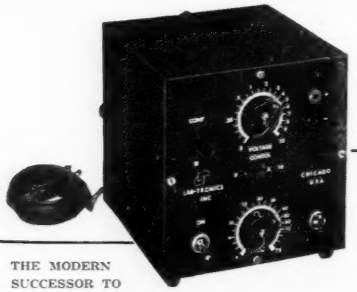

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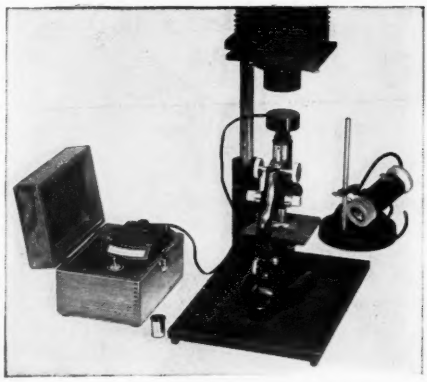

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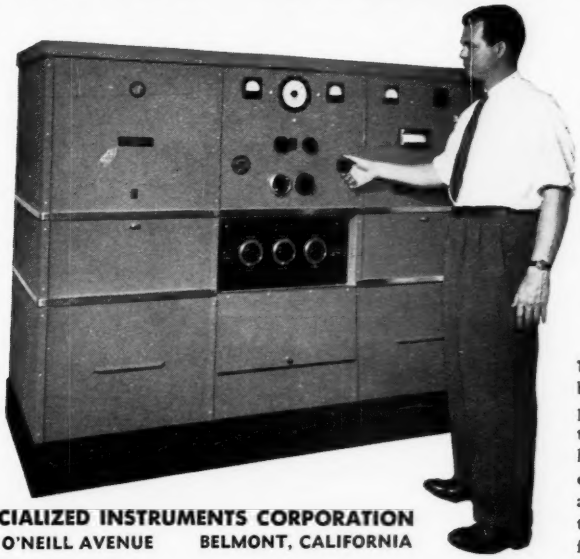

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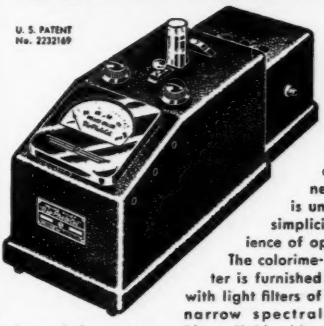

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The most manifest of the changes are the material ones. Yet even here it takes a certain perspective to see their true extent. Advances in the study of man and other living forms have extended our lifespan by decades. Discoveries in physical science have immeasurably lightened our toil, and enriched our lives. They have given leisure to an ever widening group of men. They have made a reasonable education not a special privilege, but a common right. They have made the world, in its physical dimensions, a small place, and established the means by which people in remote parts of the earth can communicate with each other, can get to know each other, and can learn to work together. They have put at the disposal of everyone the resources of physical power, of ease, and of knowledge that were in the past reserved for the few.

Not all of the changes in material well-being that science offers are realities. Yet the very fact that they are possibilities has changed the nature of the responsibility that we bear, both as individuals and as a community of men and women banded together in government. In the Greek cities, political democracy, and civilization itself, appeared possible only on the basis of a slave economy. Technology, born of science, has altered that; it has enabled mankind, as it has forced mankind, to deal with the issues of slavery as a moral issue. Poverty has always been an ugly thing, and in its extremes a desperate one. Today, it is an evil, in the sense that it lies within human hands and human hearts to abate it. Science can provide us, for the first time in history, with the means of abating hunger for everyone on earth.

Perhaps nowhere has the impact of science more clearly altered the specific terms of a great political issue than in the effects of scientific development on warfare. This is a can of worms with which I have myself unhappily been engaged for some years. It would not be honest to say—as it would be folly not to hope—that the very terror of modern weapons would in itself put an end to war; it would not even be honest to say that because of this terror the abolition of war and the maintenance of peace have become the one absolute, final objective of all political decisions. There are other things in man's life: his freedom, his decency, and his sense of right and wrong, that cannot so lightly be subjected to a single end. But what we need to remember is that war today has become, and is increasingly becoming, something very different from what it was a century ago or a millennium ago. We need to recognize the new situation as new; we need to come to it with something of the same spirit as the scientist's, when he has conducted an experiment and finds that the results are totally other than those that he had anticipated.

Four months before Hiroshima, in the last days of his life, President Roosevelt's thoughts turned to these questions. In the last words that he wrote, in words he did not live to speak, the President looked to the future, to the atomic age. He looked to the past, to the days of the founding of the Republic. He wrote:

> Thomas Jefferson, himself a distinguished scientist, once spoke of the "brotherly spirit of science, which unites into one family all its votaries of whatever grade, and however widely dispersed throughout the different quarters of the globe."
>
> Today science has brought all the different quarters of the globe so close together that it is impossible to isolate them one from another.
>
> Today we are faced with the pre-eminent fact that, if civilization is to survive, we must cultivate the science of human relationships—the ability of all peoples, of all kinds, to live together and work together, in the same world, at peace.

Science has greatly extended the range of questions in which man has a choice; it has extended man's freedom to make significant decisions. Is there anything in the methods of science itself, or in the spirit of science, that can help in the making of these decisions? To what extent is there a play on the word *science* which can mislead us and take us up false roads when we speak of this science of human relationships? Is there anything we can learn from the relevance of science to polities?

If we are to answer these questions, and answer then honestly, we must recognize important and basic differences between problems of science and problems of action, as they arise in personal or in political life. If we fail to recognize these differences, we shall be seeking magic solutions and not real ones. We shall delude ourselves into laying aside responsibility, which it is an essential part of man's life to bear.

In most scientific study, questions of good and evil, or right and wrong, play at most a minor and secondary part. For practical decisions of policy, they are basic. Without them political action would be meaningless. Practical decisions and, above all, political decisions can never quite be freed from the conflicting claims of special interest. These too are part of the meaning of a decision and of a course of action, and they must be an essential part of the force of its implementation.

Political decisions are unique acts. In politics there is little that can correspond to the scientist's repetition of an experiment. An experiment that fails in its purpose may be as good as or better than one that succeeds, because it may well be more instructive. A political decision cannot be taken twice. All the factors that are relevant to it will conjoin only once. The analogies of history can provide a guide, but only a very partial one.

These are formidable differences between the problems of science and those of practice. They show that the method of science cannot be directly adapted to the solution of problems in politics and in man's spiritual life. Yet there is relevance of a more subtle, but by no means trivial kind.

In trying more fully to explore this relevance, I should like to start with a text. This text is a letter[1] written by Thomas Jefferson to a young man who had enquired of him as to the usefulness of his studies of science. It was written in the middle of the year 1799, the year in which Napoleon abolished the Directory and began to assume dictatorial power in France, the year before Thomas Jefferson was elected for the first time as President of the United States. Jefferson and the diverse brave and hopeful men who with him laid the foundations of our own government had learned much from the peoples of other nations. Many of their highest political ideals and their most powerful political instruments were built on the experience, the insight and wisdom of European scientists and philosophers. Even today we need to remember that this was so, and that there may be much that we can learn from others, and that we should be glad to learn, as in turn by example we should be glad to teach.

Jefferson's letter starts with a survey of the subjects in science which he believes young Munford ought to pursue. I will quote one characteristic passage which may strike a familiar and homely note for you:

> The science of calculation also is indispensible as far as the extraction of the square and cube roots; Algebra as far as the quadratic equation and the use of logarithms are often of value in ordinary cases: but all beyond these is but a luxury; a delicious luxury indeed; but not to be indulged in by one who is to have a profession to follow for his subsistence.

But that is not really the part of Jefferson's letter which I commend to you. Here it is:

> I am among those who think well of the human character generally. I consider man as formed for society, and endowed by nature with those dispositions which fit him for society. I believe also, with Condorcet, as mentioned in your letter, that his mind is perfectible to a degree of which we cannot as yet form any conception. It is impossible for a man who takes a survey of what is already known, not to see what an immensity in every branch of science yet remains to be discovered, and that too of articles to which our faculties seem adequate.

And later, in the same letter, still more explicitly:

> . . . and it is still more certain that in the other branches of science, great fields are yet to be explored to which our faculties are equal, and that to an extent of which we cannot fix the limits. I join you therefore in branding as cowardly the idea that the human mind is incapable of further advances. This is precisely the doctrine which the present despots of the earth are inculcating, and their friends here re-echoing; and applying especially to religion and politics; "that it is not probable that any thing better will be discovered than what was known to our fathers." We are to look backwards then and not forwards for the improvement of science, and to find it amidst feudal barbarisms and the fires of Spitalfields. But thank heaven the American mind is already too much opened, to listen to these impostures; and while the art of printing is left to us, science can never be retrograde; what is once acquired of real knowledge can never be lost. To preserve the freedom of the human mind then and freedom of the press, every spirit should be ready to devote itself to martyrdom; for as long as we may think as we will, and speak as we think, the condition of man will proceed in improvement. The generation which is going off the stage has deserved well of mankind for the struggles it has made, and for having arrested that course of despotism which had overwhelmed the world for thousands and thousands of years. If there seems to be danger that the ground they have gained will be lost again, that danger comes from the generation your cotemporary. But that the enthusiasm which characterizes youth should lift it's parracide hands against freedom and science would be such a monstrous phaenomenon as I cannot place among possible things in this age and this country.

To me there are two striking impressions this letter of Jefferson's makes, even beyond its eloquence and its

[1] I am indebted to Dr. Julian Boyd, of Princeton University, for the copy of this hitherto unpublished letter.

beauty. The first is that the letter is pervaded with the idea of progress, that ideal that owes so much to the development of science and that in turn has provided the great enriching human faith in which scientific discovery and invention has flourished. Jefferson is confident that an increased understanding of the world will lead to progress; he is convinced that the barbarisms of the past cannot stand up against enquiry and understanding and enlightenment; he is confident in man and sure that as men know more they will act more wisely and live better. In our contemporary expressions of hope that catastrophe could be averted and civilization yet be saved, that confidence has lost much of its robustness.

The second point is that for Jefferson there is something in the ways of science that is relevant to political life. Even in religion and politics, he holds that it is probable that things better will be discovered than what was known to our fathers. This conviction that new knowledge is possible, and that not all the answers are known, is of course the stuff of the day-to-day life of the scientist. Science itself does progress; new knowledge is possible; and new knowledge, because it does not destroy or ignore the old, can only increase our understanding. The very idea of the development of science is an example of progress, and of progress which in no true sense can ever be reversed. But this is only part of the story. It is true, as Jefferson knew, that, in the large, science has flourished in conditions of human freedom, and that its growth is parallel to the growth of democratic institutions. Today, looking back on more than a century and a half of further history, we can be even more sure of this. We have seen not only the inspiriting example of science and democracy flourishing together, but the tragic examples of their foundering together. We express the hope that of this tragedy we shall soon have seen the end.

What are these lessons that the spirit of science teaches us for our practical affairs? Basic to them all is that there may be no barriers to freedom of enquiry. Basic to them all is the ideal of open-mindedness with regard to new knowledge, new experience, and new truth. Science is not based on authority. It owes its acceptance and its universality to an appeal to intelligible, communicable evidence that any interested man can evaluate.

There is no place for dogma in science. The scientist is free to ask any question, to doubt any assertion, to seek for any evidence, to correct any error. Where science has been used in the past to erect a new dogmatism, that dogmatism has found itself incompatible with the progress of science; and in the end, the dogma has yielded, or science and freedom have perished together.

Our own political life is predicated on openness. We do not believe any group of men adequate enough or wise enough to operate without scrutiny or without criticism. We know that the only way to avoid error is to detect it, that the only way to detect it is to be free to enquire. We know that the wages of secrecy are corruption. We know that in secrecy error, undetected, will flourish and subvert.

Let me be clear. Science is not skepticism. It is not the practice of science to look for things to doubt. It was not by deliberate attempt of skepticism that physicists were led to doubt the absolute nature of simultaneity, or to recognize that the ideas of strict causality embodied in classical physics could not be applied in the domain of atomic phenomena. There is probably no group of men who take more for granted in their daily work than the scientists. Common sense, and all that flows from it, is their principal basis for what they do in the laboratory and for what they make of it on paper. But for scientists it is not only honorable to doubt, it is mandatory to do that when there appears to be evidence in support of the doubt. In place of authority in science, we have and we need to have only the consensus of informed opinion, only the guide of example. No scientist needs to order his colleagues to use a new technique of experiment or to enter a new field of discovery. If he has done this, it will be an invitation to his fellows to follow.

These then are some of the attitudes of mind, these are some of the disciplines of spirit, that grow naturally in the scientist's world. They have grown there in part as a result of a humane and liberal tradition in political life, and in part as a cause of that. The open mind, the reliance on example and persuasion, rather than on authority—these are the heritage of the centuries in which science has altered the face of the earth. Science can help in diverse ways in preserving and extending this heritage. Its very universality speaks across frontiers to make truth manifest in lands otherwise darkened; its material applications create the preconditions—in leisure, in education, in means of communication—for the converse of men with each other. Science provides the material and the intellectual basis for a world in which example and understanding can help all men to fulfill their hopes. Today we need to remember that our country, founded on these practices, and grown strong by their exercise, owes its strength to them. In this time of crisis, we need to cherish that strength.

Based on an address given at the Awards Banquet of the Ninth Annual Science Talent Search in Washington, D. C., March 6, 1950.

Technical Papers

Sudorific Action of Adrenalin on the Human Sweat Glands and Determination of Their Excitability

Masao Wada

Physiological Laboratory of Tohoku University, Sendai, Japan

Although there is a vast amount of information concerning the responses of the human sweat glands to nervous, thermal, or chemical stimuli, our knowledge regarding the excitability of these glands is very scanty for lack of adequate methods of investigation. Numerous difficult problems of the physiology and pathology of the sweating mechanism, problems still unsolved, can be approached from a new angle by investigating the excitability of the sweat glands.

Recently we have devised a new method (*3*) which has two advantages over Minor's widely used method (*1, 2*): first, the sweat secretion from individual glands can be visualized directly by black spots at the sweat pores of the skin; second, the secretion in minute quantity can be detected with certainty by preventing its evaporation.

Our method will be described briefly. The area of the skin to be examined is painted with 2% or 3% iodine-absolute alcohol solution and dried completely. Then this area is painted again with a mixture of 50 to 100 g fine starch powder and 100 ml castor oil. For observation with great precision, it is desirable to limit the starch grains to about 10 μ in diameter. When sweating occurs, spots or rings of black-stained starch grains appear at the pores of functioning sweat glands and can be seen in a transparent layer of the starch-castor oil mixture, with the magnifying lens or naked eye. The usefulness of this method is illustrated in Fig. 1. The duration and cessation of sweating can be determined by repeatedly wiping the sweat spots with a dry cloth and painting with the starch-castor oil mixture. The secretion of sweat in such a small quantity as 0.00005 mg from one gland suffices to make a sweat spot visible to the naked eye.

Beginning with the work of Elliott, a number of investigators have found a local inhibitory action of adrenalin on spontaneous sweating, but have failed to find its sudorific action on the human sweat glands. Thus, it has become accepted as general knowledge that human sweat glands are not stimulated by adrenalin and this has provided a basis for the concept that the sweat glands in man are innervated by the sympathetic cholinergic nerve fibers. On the other hand, some authors have reported that under certain conditions sweating is elicited by adrenalin, but these findings have been rejected or considered to be not convincing.

Contrary to the accepted view, we have recently demonstrated with certainty by our method a sudorific effect of adrenalin applied intradermally. Adrenalin hydrochloride solution (Sankyo Co., synthetic, $1:10^3$) was diluted with 0.9% sodium chloride solution to various concentrations and 0.1 ml or 0.2 ml was injected into the skin of the forearm, dorsum of the hand, or other regions of the body. With adrenalin of $1:10^3$ to $1:10^4$, sweating began to appear over and around the injection wheal within 1–2 min after injection and spread progressively by forming processes or branches of sweat spots, along with expansion of the anemic area, showing diffusion of adrenalin via the lymphatic channels. As sweating became more evident, the sweat spots increased in size. This sweating response reached its maximum in 1–1½ hr and then declined until it ceased, 4–5 hr after injection. Local anemia generally persisted longer than the sweating. The extent and duration of sweating depended on the concentrations of adrenalin used. The minimal effective concentration for causing sweating on the forearm of the majority of the young healthy subjects tested was $1:10^7$. With such a threshold concentration, the sweat spots disperse evenly over the original wheal of injection (Fig. 1). The sudorific effect of adrenalin was not due to the fluid in which it was dissolved. Injections of 0.9% NaCl solution or HCl solutions of pH corresponding to that of the adrenalin solutions were without effect. When adrenalin was destroyed by ultraviolet rays or by alkali, its stimulating action on the sweat glands was lost. The sweating response to adrenalin was not inhibited by atropine. Cocaine also had no influence on it.

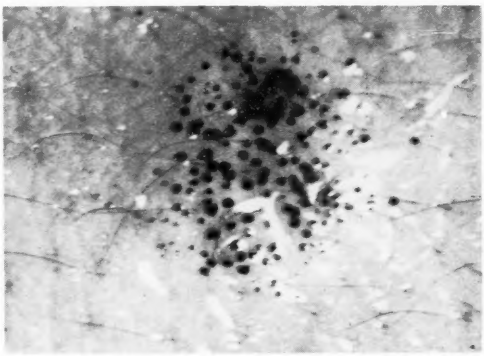

FIG. 1. Sweat spots at individual sweat pores of the extensor surface of the forearm following intradermal injection of adrenalin of $1:10^7$. Photographed 18 min after injection; ×4. Not retouched. The white spots are caused by reflection of light.

By determining the minimal effective concentration of adrenalin applied intradermally, we have attempted to measure the excitability of the sweat glands (*4*). This was expressed as usual by the reciprocal (or its logarithm) of the threshold concentrations of adrenalin. The excitability of the glands on the forearm thus measured was, as described above, 10^7 in more than 80% of the healthy males and females tested, aged 14 to 24

yr, and it was 10^6 in the remaining subjects. An excitability of 10^5 was rarely found. The sweat glands of the arm, leg, and trunk exhibited about the same excitability. No seasonal variation in the excitability was found, as measured by the adrenalin method, in the healthy adult subjects, at environmental temperatures of 4° to 27° C. In younger subjects, aged 1 to 12 yr, and in older subjects aged 62 to 77 yr, the excitability was found to be much lower. In the majority of the children of 1 to 5 yr, sweating was not produced even with adrenalin of $1:10^4$. These findings indicate that the excitability of the human sweat glands reaches its highest level at the age of about 14 yr in both sexes, but decreases in senility. However, it must be noted that the sweat glands of newborn infants tested within one week after birth exhibited almost the same excitability as that of their puerperal mothers (Nagashima). Whether some hormone or humoral agent exists for increasing the excitability of the sweat glands and maintaining it at high levels, remains to be decided by further investigations.

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Two Crossover-Selector Systems: New Tools in Genetics

Maurice Whittinghill

Department of Zoology, University of North Carolina, Chapel Hill

The current interest in mutation rate as a fundamental biological process might well be paralleled by the study of a related process, namely, crossing over. Not only does a single agent, irradiation or heat, affect both processes, but crossing over itself produces some mutants (*1, 2*). Therefore the finding that a new agent, chemical or physical, is an inducer of crossing over greatly increases the probability that the same agent will turn out to be mutagenic, and vice versa. Mutation studies are intrinsically laborious, although special methods have been devised by H. J. Muller and others both to speed and to improve the search for mutagenic agents and conditions in *Drosophila melanogaster*. Whereas mutagenic agents may act with a frequency of about 1×10^{-4}, crossover inducers may act to the extent of 1×10^{-2} or 1×10^{-1}. Hence a short way to find a new mutagen among several substances might be through first demonstrating its effect upon crossing over.

The availability of a new and rapid way of finding crossovers among large numbers of zygotes, to be described here, confirms the strategy of investigating the many genetically interesting chemicals, such as carcinogens, by screening for the induction of crossing over in advance of more extensive experiments on their possible mutagenic properties. However, the usual studies on changes in apparent crossing over in *Drosophila* females are subject to previously unappreciated sources of error (*3, 5*). This suggests that more exact data may be obtained from studies on the induction of crossovers in heterozygous males, where none are normally expected, but such experiments have usually been almost as laborious as mutation studies. The present paper describes two plans to simplify the detection of crossovers. The first plan has been implemented by five special stocks, some of which have required two years to synthesize and are at present propagated only at the University of North Carolina.[1]

The first plan eliminates all noncrossover offspring, which may represent 99% of a whole experiment and even 100% of many families within the test. The 1% remaining, an average frequency for crossovers in a successful induction experiment, develop freely. The plan requires four dominant genes, each of which is lethal to egg or larva when homozygous. Two of the lethals must be closely linked in coupling phase on one side of the spindle attachment (see genotype of ♂ in Table 1), and the other two should be located in the opposite arm of the homologous chromosome and as close together as possible. The mutants Minute(3)y, Glued, Stubble, and bithorax-Dominant, at loci 40.2, 41.4, 58.2, and 58.8, respectively, meet these requirements. Such a stock is fertile, and provides the males for experimental purposes. Females used in place of a recessive test-cross stock have the alternated arrangement of the same lethals, as shown in Table 1, or else *My* bx^D*/Gl Sb*, either of which is easily carried in balanced stock. When experimental matings are made the nonecrossover zygotes all die: one quarter of them are killed by homozygous *My/My*, another quarter by *Gl/Gl*, a third quarter by *Sb/Sb* and the remaining noncrossovers by bx^D/bx^D. Most spontaneous crossovers are also killed by one or more of these combinations, but the wild type crossovers formed in males will survive. Table 1 includes only noncrossovers and single crossovers, and it omits gametes expected less often than 0.3% of the time. The full checkerboard would be 16×16 and would contain 256 kinds of zygotes. These have been figured out, and no confusion as to the origin of any adult will result unless triple crossover wild type eggs, probability 1.6×10^{-6}, are formed.

Thus the vast majority of the F_1's die, in egg or larval stages in this illustration, and the crossovers, although rare, become very conspicuous as the only adults. The need for classification of the adults under the microscope is directly proportional to the success of the inducing agent. Classification determines whether a crossover contains two dominant mutant markers, expected in most instances of male-formed crossovers (top half of Table 1), or an odd number of dominants, expected from the rare female-produced crossovers, which affect only 0.3% or 0.6% of the eggs. Test-crosses to wild may verify any doubtful classes of crossovers.

[1] Grateful acknowledgment is made for two grants from the Carnegie Research Fund of the University of North Carolina to assist in the making of stocks.

This method has been used successfully, in its first extensive test, at the Biology Division of the Oak Ridge National Laboratories in a gamma ray study (*4*) employing the three *My Gl Sb bx*^{D} stocks mentioned. There was very little trouble from mold growth in spite of the paucity of large larvae. Culture conditions for the eclosion of one or more crossover individuals must have been satisfactory, because one quarter of the fertile irradiated males produced them and because even three-week-old cultures could produce adult flies if reseeded with wild type zygotes.

TABLE 1

GENOTYPES OF SURVIVING ADULTS FROM THE LETHAL SYSTEM OF CROSSOVER-SELECTOR MATINGS

$\frac{My}{Gl}\ \frac{Sb}{bx^{D}}$ females by treated $\frac{My\ Gl}{Sb\ bx^{D}}$ males

	Sperms				
Eggs: frequency and kinds	noncrossovers				crossovers, if any
	My Gl	*Sb bx*^{D}	*My Gl Sb bx*^{D}	+	
%					
41 *My Sb*					*My Sb*/+
41 *Gl bx*^{D}					*Gl bx*^{D}/+
8 *My bx*^{D}					*My bx*^{D}/+
8 *Gl Sb*	All these combinations die except				*Gl Sb*/+
0.6 *My Gl bx*^{D}					*My Gl bx*^{D}/+
0.6 *Sb My Gl*/*Sb*					*Sb*/+
0.3 *My Sb bx*^{D}	and				*My Sb bx*^{D}/+
0.3 *Gl*		*Gl*/*Sb bx*^{D}			*Gl*/+
Fate of zygotes, by sperm classes:	99.4% die;	99.7% die;	all die;		all survive, if formed

Other less effective but potentially useful stocks marking the second chromosome in a crossover-selector system have also been synthesized. These were *S*^{W} *Cy*/*Pfd L*^{2} to provide males and *S Pfd*/*Cy L*^{4} to provide females for the test matings. A certain percentage of the *L*^{2}/*L*^{4} flies emerged and had to be classified along with crossovers; hence this implementation of the system was less successful, although it was superior to ordinary test-crossing. Homozygous Curly flies were encountered only three times but caused no confusion. The other homozygotes always died, as intended.

While the above stocks were being synthesized, a second plan was devised and found adequate. It delays noncrossovers but does not kill them. Two different Minute mutants are used because Minutes extend the period from egg to adult by two or more days at 25° C. Heterozygous males are obtained carrying Minute(3)y in the left arm of one chromosome and Minute(3)y in the right arm of the other chromosome (Table 2). When these are crossed to normal females all noncrossover offspring will be Minute, either *My* or *Mw*, and will require 12 days to become imagoes. Single crossovers formed between the two loci will be wild type or will have both Minute genes. The latter are not detected, but the wild type chromosomes, comprising one-half the products of crossing over, will emerge in about 10 days, as shown in Table 2. Therefore experiments on *My*/*Mw* females, and on similar males, were set up with daily transfers of parents followed on the 10th and 11th days by inspection to see whether any adults were present. The flies found on these days were etherized and inspected to make sure that they were wild type. The cultures were discarded when the mass of noncrossovers began to appear on the 12th day. Cultures from *My*/*Mw* females did have adult flies, all wild type, on the 10th and 11th days due to normal crossing over in the female, whereas untreated *My*/*Mw* males had no offspring until the noncrossovers, all Minute in phenotype, emerged on the 12th day. Because the heterozygotes for this method are simpler to obtain, this second method may be more generally useful

TABLE 2

KINDS OF ADULTS SORTING OUT AT DIFFERENT TIMES FROM A ONE-DAY TRANSFER IN TEST-CROSSES OF BALANCED MINUTES

Treated $\frac{My}{+}\ \frac{+}{Mw}$ male × wild stock

Time when culture is observed	Gametes						Summary
	noncrossovers				crossovers		
	My +		+ *Mw*		*My Mw*	+ +	
10th day	0		0		0	wild	Crossovers,
11th day	0		0		0	wild	if formed
12th day	Minute		Minute		Minute	0	Chiefly or entirely noncrossovers

In other species where the selection of mutants is not broad enough, as indeed it just barely is in *Drosophila melanogaster*, to employ the lethal scheme first described.

In view of present interest in the action of carcinogens and other chemicals upon mutation, the available sets of stocks and the above plan may promote certain investigations which might proceed more slowly if studied by mutation techniques. Whereas mutation studies have reduced the classification to the objective level of recognizing the complete absence of males among the progeny (the *ClB* method) or the absence of wild type males among apricot Bar flies (the Muller-5 method), the crossover-selector system requires mainly that the experimenter shall notice one or more adults when inspecting culture vials which have had larvae in them. Because of the more rapid scoring of test vials, and a slightly greater ease of inducing crossovers than of inducing mutants, the crossover-selector system may very well take its place among modern techniques of *Drosophila* genetics for studies with chemical agents and with irradiation treatments.

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The Mass of Gastric Mucosa Cells Measured by X-Ray Absorption

Arne Engström and David Glick[1, 2]

Department for Cell Research, Karolinska Institutet, Stockholm, Sweden

It was previously shown (*2*) that the utilization of selected bands in a long wavelength, continuous x-ray spectrum makes it possible to determine the dry weight of single cells and cell structures by absorption measurements. A consideration of the theory of x-ray absorption revealed that the mass of a structure in biological material might be determined with an error of less than 5% even if there were relatively large variations in the proportion of the constituent elements. Calculations showed that a great change in carbon, nitrogen, or oxygen content (in the case of nitrogen up to 60%) produces an error of only 5% in the mass determination. The same error will occur if other elements such as phosphorus, sulfur, chlorine, and calcium are present in very high concentrations; i.e., the concentration of phosphorus would have to be about 5%, sulfur 14%, chlorine 17%, and calcium 9%. Thus only in special instances, e.g., calcified tissues, need a correction for other elements, with the exception of hydrogen, be made. The correction for the absorption of hydrogen is calculated by means of a formula derived for the purpose (*1, 3*), and this correction is less than 10%. Mass can be determined by x-ray absorption technique with an over-all error under 10%.

In the present study the absorption measurements were applied to the determination of the dry weight of the cells of dog gastric mucosa from an animal which had been given a series of intramuscular injections of histamine in beeswax to produce a chronic hyperacidity. One injection of 30 mg was given daily for 45 days, and on the last day 40 mg of nembutal per kg was administered intravenously to kill the dog, and the tissue was removed. The dog was one of a group used for another study by D. J. Ferguson, of the Surgery Department of the University of Minnesota, and we are indebted to him for the material. Small pieces of gastric mucosa from the fundus were quickly dissected, immediately frozen in isopentane cooled by liquid air, placed on a block of previously degassed paraffin in a freezing-drying apparatus and dehydrated at about −80° C and 10^{-6} mm mercury pressure for a week. The frozen-dried tissue was infiltrated with paraffin in the apparatus; air was admitted to the system only after the tissue was submerged in the molten parafin.[3] Sections were cut at 4 μ to 7 μ, placed directly over the slits in the brass disks supporting tissue during measurement, and deparaffinized with xylol.

TABLE 1

DRY WEIGHTS OF DOG GASTRIC MUCOSA CELLS

	Dry wt (g $10^{-12}/\mu^2$) ± standard error of mean				Dry wt (g $10^{-12}/\mu^3$)			Mass ratios		
	Mean of whole chief cell area	Mean of epithelial cytoplasm (secretion-free)	Mean of whole parietal cell area	Thickness (μ)	Mean of whole chief cell area	Mean of epithelial cytoplasm (secretion-free)	Mean of whole parietal cell area	Chief	Epithelial	Parietal
Frozen-dried section	1.5 ± < 0.1	1.2 ± < 0.1	0.6 ± < 0.1	4.7	0.3	0.2–0.3	0.1	2.5	2.0	1
" " "	2.7 ± 0.1	2.0 ± < 0.1	0.9 ± < 0.1	..	..	.....	..	3.0	2.2	1
" " "	2.1 ± 0.1	1.5 ± < 0.1	0.9 ± < 0.1	..	..	.....	..	2.3	1.7	1
" " "	2.2 ± 0.1	1.5 ± < 0.1*	0.9 ± < 0.1	7.0	0.3	0.2	0.1	2.4	1.7	1
Formalin-fixed section	1.7 ± < 0.1	1.5 ± < 0.1	0.9 ± < 0.1	7.6	0.2	0.2	0.1	1.9	1.7	1
" " "	2.3 ± < 0.1	2.0 ± 0.1	1.2 ± < 0.1	7.6	0.3	0.2–0.3	0.1–0.2	1.9	1.7	1

* The secretion in the upper part of the epithelial cells had a mass of $3.3 \pm 0.1 \cdot 10^{-12}$ g/μ^2 which corresponds to $0.5 \cdot 10^{-12}$ g/μ^3.

In order to observe the effect on cell mass of formalin fixation and alcohol dehydration as applied routinely for histological preparations, the block of embedded frozen-dried tissue left after the sections were removed for absorption measurements was deparaffinized in xylol, hydrated through graded alcohols, and placed in 10% formaldehyde overnight. This was followed by dehydration in alcohols, paraffin infiltration, sectioning, and measurement of x-ray absorption in the same manner as used for the frozen-dried material.

Measurements were made following the technique described (*1–3*). X-rays (3000–4000 volts), filtered through an aluminum foil 9 μ thick, were employed. This gave a beam with maximum intensity at 8–12 A. Lippman photographic film (Gevaert, Antwerp), which has a resolving power of about 1 μ, was used to record the radiation intensities. Each microradiogram also included a simultaneous exposure of a mass reference system consisting of two strips of a thin nitrocellulose film. The microradiogram of the sample and reference system was enlarged 200 to 600 times by photomicrography, using constant illumination. By photometric measurements of small areas (0.5 mm²) in the enlarged images, the x-ray

[1] Supported by The Commonwealth Fund.

[2] Present address: Department of Physiological Chemistry, University of Minnesota, Minneapolis.

[3] We are indebted to Mr. B. Malmstrom for preparing the paraffin blocks.

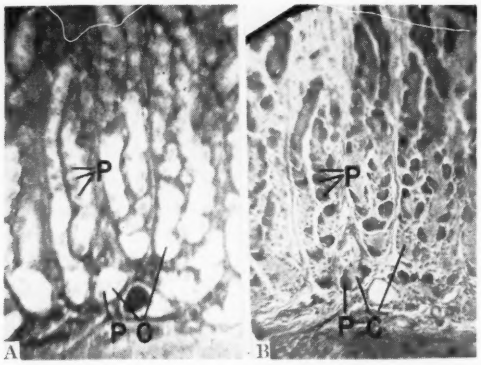

FIG. 1. (A) Microradiogram of section of frozen-dried gastric mucosa, 130×. The lighter the area the greater the absorption of x-rays. (B) Photomicrograph of same section after staining. Parietal cells (P) have least absorption and chief cells (C) the greatest.

absorption in the cells was compared to that in the reference system, and the mass per unit area was calculated. From approximations of the thickness of the sections employed, estimates of mass per unit volume were made.

masses of the various cells may be seen in Figs. 1 and 2. The photometric measurements were made on the secretion-free cytoplasmic area of the epithelial cells in the enlarged microradiogram. The nuclei were too small to permit reliable measurements, but it can be seen by inspection that they show less absorption than the secretion-free cytoplasm, while the secretion itself within the cytoplasm has the greatest absorption. Nuclei in parietal and chief cells could not be distinguished in the photographs, so that measurements were made on whole cells. Usually ten cells of each type in a photomicrogram were measured photometrically, and the means, with their standard deviations, were calculated. Thickness measurements on the sections were made with the micrometer screw of a microscope which was used with oil immersion. Since the thickness could be determined only approximately, the calculations of dry weight per unit volume do not have as great accuracy as those of dry weight per unit area, and accordingly the standard deviation was not estimated for dry weight per unit volume.

It is apparent from these experiments that the mucus- and enzyme-secreting cells have a greater mass than those secreting acid. The greatest variability in mass was found in the chief cells, and this may have been due to the cells' being in different stages of secretory activity.

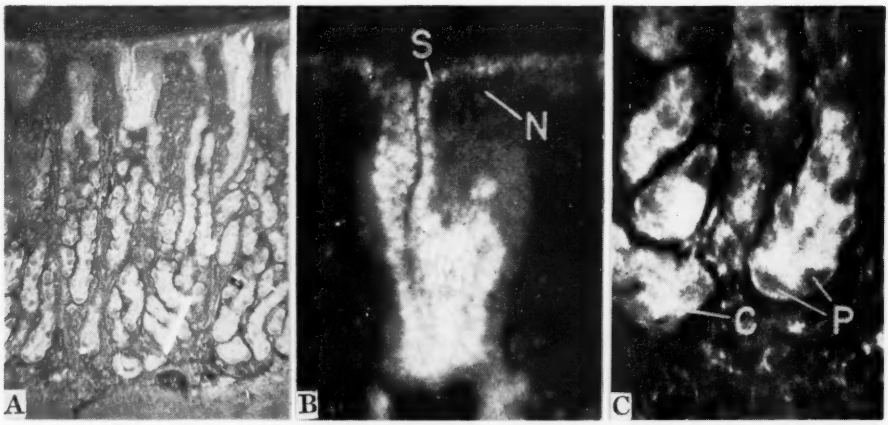

FIG. 2. (A) Microradiogram of section of frozen-dried gastric mucosa, 88×. (B) Microradiogram of epithelial cell area in same section, 330×. Nuclei (N) of epithelial cells have less absorption than the cytoplasm. The secretion (S) above the nucleus has strong absorption. (C) Microradiogram of parietal and chief cell area in the same section. The chief cells have greater absorption than the parietal cells, and nuclei cannot be seen in either.

After the microradiograms were obtained, the same sections were stained with hematoxylin and eosin without removing them from the brass disks, and photomicrographs were taken having the same enlargement as that used for the microradiograms. The photograph of the stained tissue facilitated identification of individual cells in the enlarged radiograms.

Results of the measurements are given in Table 1. The nitrocellulose films employed as mass reference weighed 0.350 mg/cm², and the elementary composition was: C, 46.7%; N, 6.6%; O, 41.4%; H, 5.3%. A factor was calculated as described (*1*, *3*) to convert the absorption of substance of this composition to mass. The relative

The formalin fixation and alcohol treatment processes routinely used for histological preparations effected a loss in mass of the chief cells, as shown by the mass ratios in Table 1, indicating that the protein denaturation did not prevent solution of a certain amount of the cellular material.

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The Control of Survival Time of Mice Bearing Methylcholanthrene-induced Fibrosarcomas[1]

Leonell C. Strong

Department of Anatomy, Yale University School of Medicine, New Haven, Connecticut

Data have been published which indicate that the rate at which fibrosarcomas appear at the site of the injection of methylcholanthrene into mice (frequency incidence) varies with the litter sequence of a given female (*1*). The susceptibility to chemically induced fibrosarcomas is lowest in mice of the first and second litters and highest in mice of the fifth and sixth litters. The increase of susceptibility in the succeeding litters of a single female mouse has also been shown to be variable, being very small in mice of some stocks and significantly higher in mice of other stocks. Increased susceptibility to fibrosarcomas of later litters is probably not associated with heterosis, since it has been found in mice of inbred strains as well as in mice of an F_1 generation that were obtained by a cross between the inbred Brs subline and the C_{57} blacks as originally determined.

The pBr subline (one of the major sublines of the NHO descent) has been continued for 26 generations by a continuous process of selection for greater resistance to methylcholanthrene-induced fibrosarcomas following the subcutaneous injection of this carcinogen into both parents at 60 days of age. The latent period for the appearance of chemically induced tumors has been increased by such selection from 125 days to 436 days in 22 generations. The pBr methylcholanthrene-treated descent is still being continued.

The pBrunt subline was separated from the pBr-treated series in the F_{17} generation of brother-to-sister matings, at a time when the average latent period for the appearance of induced fibrosarcomas was 363 days. The subline was then continued as an untreated descent. The 2pBrunt subline was separated off in the F_{20} generation, when the average latent period for induced fibrosarcomas was 393 days; this new subline was similarly continued as another untreated descent. Mice of the 2pBrunt subline thus have a greater resistance to the appearance of fibrosarcomas than mice of the pBrunt subline, and this greater resistance is measurable in terms of an increased average latent period (393 days compared to 363 days). After several generations of untreated descent, the offspring of mice of the two descents (the pBrunt and the 2pBrunt) are now being injected with 1 mg of methylcholanthrene dissolved in 0.1 ml of sesame oil at 60 days of age. Unpublished data show that mice of the two descents are different not only in the rate at which fibrosarcomas appear at the site of injection of the methylcholanthrene, but also in survival time (time between the appearance of the chemically induced fibrinosarcomas and the death of the individual).

[1] This experiment has been made possible by grants from The Anna Fuller Fund and The Jane Coffin Childs Memorial Fund for Medical Research.

TABLE 1

AVERAGE LATENT PERIOD AND AVERAGE SURVIVAL TIME FOR MICE OF THE PBRUNT SUBLINE*

Litter	No. of mice	Latent period	Survival time
1	9	90.3	52.0
2	23	88.2	60.7
3	22	79.7	74.3
4	40	84.3	90.1
1–4	94	84.8	75.5
5	35	68.0	101.1
6	20	85.6	107.0
7	22	82.7	106.6
8	7	85.0	130.0
5–8	84	77.3	106.3
1–8	188	81.4	85.3

* Only mice with latent periods less than 100 days are included.

In this paper data will be given only on the survival time of female mice of the pBrunt subline, which develop induced fibrosarcomas with a latent period of less than 100 days. These data, summarized in Table 1, are presented graphically in Fig. 1. The mice are classed according to the ordinal numbers of the litters to which they belong, beginning with the first and ending with the eighth.

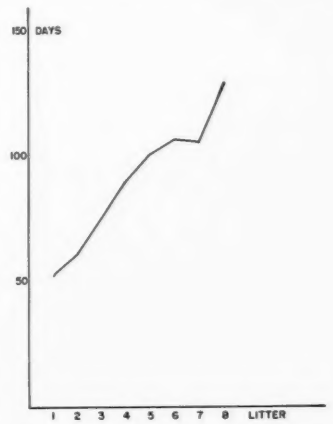

FIG. 1. Litter frequency is given on the base line and the average survival times of mice bearing induced fibrosarcomas are given on the vertical line expressed in days.

An analysis of the data indicates that the survival time of a mouse of the pBrunt descent growing an induced fibrosarcoma increases with the litter frequency of the mother. The group of mice that survive for the shortest length of time (an average of 52.4 days) with the growth of a primary induced fibrosarcoma belong to a first litter. This survival time gradually increases with litter frequency, until, if the mouse belongs to an eighth litter, the average survival time is 130.0 days. After temporary growth, 16 mice belonging to advanced litters have regressed their primary chemically induced fibrosarcomas spontaneously.

Mice of the pBrunt descent growing primary induced fibrosarcomas thus have a greater resistance to the growth of this type of malignant tumor than mice of the C_{57} stock, which under the same conditions survive on the average only 30 to 40 days.

By controlling the ordinal position of the litter in which a mouse has been born, an influence on survival time with growth of a malignant tumor has been determined.

It is difficult to obtain many mice that belong to litters succeeding the eighth one. Later litters should yield interesting data about the growth rates of chemically induced fibrosarcomas, retrogressive potentialities, alterations in latent period, survival time, and perhaps in the histological characteristics, invasiveness, and ability of the tumors to metastasize.

Only a short time ago it was felt that the growth of a malignant tumor was autonomous, that it grows and kills an individual by laws yet unknown. We are now able to determine, to no slight degree, the end results of the growth of a malignant tumor, at least in a carefully controlled experimental animal. Through the construction by genetic principles of a biological system that shows increased resistance to the growth of a malignant tumor, such as obtained in the pBr subline, the fate of the individual can be changed significantly.

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A Synthetic Diet for the Biological Assay of Thiamine

Carmen Ll. Intengan, Hazel E. Munsell, and Robert S. Harris

Nutritional Biochemistry Laboratories, Massachusetts Institute of Technology, Cambridge, Massachusetts

Recently these laboratories undertook to determine the thiamine content of rice bran, using the biological method of assay described in the U. S. Pharmacopoeia XIII (*7*). This method is the one most commonly employed in making determinations of thiamine content by the biological procedure.

Twenty weanling rats were placed in cages having wire screen bottoms to prevent access to feces, and were given the basal diet ad libitum. These animals failed to develop polyneuritis in the expected manner. Because of the possibility that autoclaving for the prescribed 5 hr had not destroyed the thiamine naturally present in the yeast and peanut components of the U.S.P. ration, a second batch of each was autoclaved for 7 hr and a new lot of diet satisfactorily prepared. Still the rats failed to develop polyneuritis.

A study was then made of a "synthetic" ration, which was essentially devoid of thiamine and yet contained liberal amounts of all other nutrients known to be required by the rat. It is now recognized that rats maintained on a thiamine-free diet die of inanition without symptoms of polyneuritis (*2–5*), whereas those given small amounts (0.25–0.75 μg per rat per day) of the vitamin develop typical symptoms proportional in severity to the thiamine intake (*1–6*). Ammerman and Waterman (*1*) found that 0.5 μg of thiamine hydrochloride per rat per day, given in conjunction with a vitamin B_1-free diet, produced paralysis in 70% of the animals in 5–8 weeks. Supplee *et al.* (*6*) used 0.75 μg vitamin B_1, 10 μg lactoflavin, and 100 mg autoclaved rice polish concentrate as a supplement to the basal vitamin B_1-free diet, and observed that some animals showed prolonged resistance to development of polyneuritis.

The composition of the synthetic diet used in the present study was:

sucrose	55.5%
vitamin-free casein	27.0%
salts (Hubbell)	3.0%
Crisco	14.0%
vitamin mixture	0.5%.

The vitamin mixture contained, in mg per 0.5 g: riboflavin 0.5, pyridoxine 0.4, niacin 2.0, calcium pantothenate 2.0, *p*-amino benzoic acid 10.0, inositol 200.0, biotin 0.03, choline chloride 300.0, menadione 0.3, α-tocopherol 10.0, folic acid 0.25, ascorbic acid 10.0, and also 1250 U.S.P. units of vitamin A and 125 U.S.P. units of vitamin D.

This thiamine-free synthetic diet was fed ad libitum to four comparable groups of 15 weanling rats each. The animals of group I received no supplement. Those

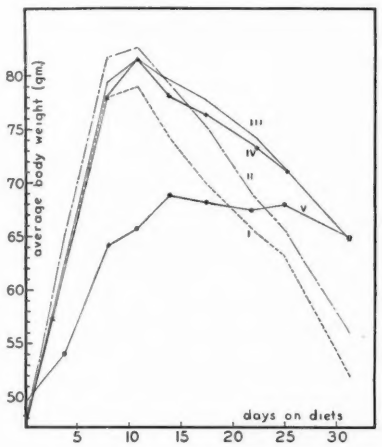

FIG. 1. Body weight during the depletion of groups of rats which eventually developed polyneuritis.

of groups II, III, and IV received, respectively, 0.25, 0.50, and 0.75 μg of thiamine hydrochloride daily, given orally as a solution delivered from a calibrated pipette. A fifth group of 23 rats was given the U.S.P. basal diet. The assays with all five groups were carried out according to U.S.P. procedure (*7*).

TABLE 1

SUMMARY OF RESULTS FROM FEEDING TRIALS WITH RATS IN A COMPARISON OF FIVE DIETS FOR THE BIOLOGICAL ASSAY OF THIAMINE

Group No. and diet	No. rats	No. rats that died without polyneuritis	Rats that developed polyneuritis		Avg No. days for development of polyneuritis	No. rats that died before completion of first assay	No. rats that failed to develop polyneuritis 2nd time	No. rats that completed one or more assay periods	No. satisfactory* assays	Percent of rats giving satisfactory results
			No.	Percent						
I Synthetic	15	5	10	67	33.5	7	0	3	3	20
II Synthetic 0.25 μg B_1	14	2	12	86	34.6	4	0	8	6	44
III Synthetic 0.5 μg B_1	14	0	14	100	37.1	1	0	13	11	79
IV Synthetic 0.75 μg B_1	15	0	15	100	44.2	1	2	12	10	67
V U.S.P.	23	0	18	78	40.1	2	3	13	10	43

* Results judged satisfactory according to the U.S.P. method—i.e., when the curative period was not less than 5 days and not more than 15 days.

During the depletion period all rats were weighed twice weekly and observed closely for symptoms of polyneuritis. Animals were considered polyneuritic and suitable for test feeding if they exhibited convulsions, paralysis, or cartwheel motion, or rolled on their backs when twirled by the tail. Rice bran and ground whole corn were used as assay materials. Each test dose was estimated to contain 6 μg (2 I.U.) thiamine hydrochloride on the basis of results from chemical analyses by the thiochrome method. During the test period all rats were weighed daily. The rats of groups I, III, IV, and V were used in successive feeding trials until most had died. Some in group II were killed at the end of the first test period in connection with another study, so that a similar record on them is not available.

The relative rates of growth during the depletion period of the rats in the several groups that developed polyneuritis are shown in Fig. 1. The maximum average weight of group V was considerably less than that of the other four groups; this may indicate that the U.S.P. basal diet contains less than optimum amounts of some nutrient or nutrients essential to rat growth. Calculation of the thiamine content of the U.S.P. diet on the basis of chemical analyses of one batch of ingredients gave a value of 4.95 μg per 100 g, indicating that thiamine was not the limiting factor.

Data pertinent to the several assay groups are summarized in Tables 1 and 2. The animals of group I showed the most sudden and rapid loss of weight. In the three rats giving satisfactory assay results, the symptoms of polyneuritis were severe, the curative periods were short, and complete cures were not obtained in all cases. The response of the animals of group II was intermediate between that of group I and the three remaining groups. The symptoms of polyneuritis were severe and the curative periods were short. In group III the rats showed a gradual decline in weight, the symptoms of polyneuritis were clear-cut and specific, and recovery followed promptly after administration of the Reference Standard or the test food. Most animals in this group served in three assay periods, although the results were not always satisfactory and the length of successive curative periods tended to diminish. The rats of group IV, like those of group III, showed a gradual decline in weight but the individuals of this group showed a wider range (36–62 days) in the time elapsing before the onset of polyneuritis than those of group III (31–43 days) and many assay results were unsatisfactory because of prolonged curative periods. The animals of group V also showed a wide range (38–71 days) in the time elapsing before the symptoms of polyneuritis first appeared, and also showed a tendency toward prolonged curative periods.

On the basis of these findings it would seem that the synthetic diet described, supplemented daily with 0.5 μg thiamine hydrochloride administered to the rats orally, is more suitable for the biological assay of vitamin B_1 than the U.S.P. diet. On this synthetic diet, 100% of the animals developed polyneuritis and it was possible to carry a high percentage through several assay periods.

The results from the feeding trials with rice bran and whole corn indicate that the thiamine content determined

TABLE 2

SATISFACTORY ASSAY RESULTS FOR RICE BRAN AND WHOLE CORN

Rat No.	Duration of curative period in days									
	Assay period No. 1		Assay period No. 2		Assay period No. 3		Assay period No. 2		Assay period No. 3	
	2 I.U. B_1	Rice bran	2 I.U. B_1	Rice bran	2 I.U. B_1	Rice bran	2 I.U. B_1	Corn	2 I.U. B_1	Corn
Group I :										
1	9	5								
2	9	10					8	6		
3	7	5								
Avg	8.3	6.7					8.0	6.0		
Group II :										
1			6	10						
2	8	15								
3	8	6								
4			7	6						
5	8	7								
6			5	9						
Avg	8.0	9.3	6.0	8.3						
Group III :										
1	7	9	6	8					7	6
2			8	8						
3									5	5
4	12	12					6	9		
5	9	11							9	7
6	8	6								
7	9	8	5	6					6	7
8	12	10								
9	9	15					8	7		
10	14	7					5	5		
11					6	7				
Avg	10.0	9.8	6.3	7.3	6.0	7.0	6.3	7.0	6.8	6.3
Group IV :										
1	10	7								
2	10	12								
3	7	8					14	11		
4	11	13								
5							9	8		
6	12	8								
7	10	10								
8	11	14					15	15		
9							9	10		
10	15	10								
Avg	10.8	10.3					11.8	11.0		
Group V :										
1	13	9					9	12		
2	15	14								
3	12	12					9	9		
4	10	13								
5							7	7		
6	14	10					10	7		
7	14	6					6	5		
8	9	12					11	13		
9	9	10								
10							8	13		
Avg	12.0	10.8					8.6	9.6		

by chemical analysis closely approximated that shown by biological assay.

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Some Properties of 2,3,5-Triphenyltetrazolium Chloride and Several Iodo Derivatives[1]

Elsie Atkinson,[2] Samuel Melvin,[3] and Sidney W. Fox

Chemistry Laboratory, Iowa State College, Ames

The vital staining properties of "tetrazole" (2,3,5-triphenyltetrazolium chloride) (*4*) and of its various derivatives have been under investigation in this laboratory for some time (*1*). An observation of partially selective staining action on sunflower tumor tissue has led to consideration of compounds in this series as neoplasm indicators, of iodo derivatives for quantitative estimation of tumor mass, and as a means of localized application of organically bound radioiodine. Various derivatives are being synthesized for possible extension of their utility in oncology, germinability, enzymology, sperm fertility, and in other applications. Two reports which have appeared from other laboratories concern behavior of 2,3,5-triphenyltetrazolium chloride (*8*) and of the 3-*p*-iodophenyl analogue in animal tumors (*7*). While such compounds serve partially as selective tumor stains, radioiodine injected in this form has not accumulated selectively in animal tumors tested (*6, 7*).

Variations noted in germinability tests (*3*) may be explained in part by the finding that whereas the triphenyltetrazolium chloride is readily prepared by the usual procedure (*9*), purification from HCl solution followed by drying in air yields the di-(tetrazolium chloride) hydrochloride hydrate. Drying at 105°–110° C for 5 hr reconverts the hydrochloride hydrate to the chloride. The added acidity due to the HCl may affect the staining ability of this material, since this property has been found to be pH-sensitive.

The tetrazole employed here has been prepared by the usual procedure (*9*) except that an amount of butyl nitrite equimolar to the isoamyl nitrite previously employed has been used.

When 2,3,5-triphenyltetrazolium chloride of mp 243° C (with decomposition) was dissolved in ten parts of warm water, precipitated with three parts of concentrated HCl solution, and allowed to dry in air, silky needles of mp 180° C with preshrinking were obtained. Some samples exhibited only partial melting. *Analysis.* Calculated for $(C_{19}H_{15}N_4Cl)_2 \cdot HCl \cdot H_2O$: N, 15.48; Cl, 14.69. Found: N (Dumas), 15.70, 15.43; Cl, 14.70, 14.58.

When a sample of this compound was dried at 105°–110° C, crystals of mp 243° C (with decomposition) were recovered. *Analysis.* Calculated for $C_{19}H_{15}N_4Cl$: N, 16.74; Cl, 10.59. Found: N, 16.77, 16.69; Cl, 10.54, 10.60. The hydrochloride hydrate could also be reconverted to the chloride by solution in alcohol and precipitation with ether. Simple washing with ether did not effect the conversion.

More rapid and more intense staining by iodo tetrazoliums (*2*) than by the parent compound was observed in numerous experiments. In corn germinability tests, the times for first visual recognition are noted in Table 1. The solutions employed were 0.05% by weight and were read by an observer unacquainted with the contents of the solutions. The corn was a sample of high germinability. The nitro compound proved not only to be the most rapidly reactive of the group, but also permitted more rapid visual differentiation of the tissues within the embryo.

TABLE 1

TIME FOR REDUCTION OF TETRAZOLIUM SALTS BY CORN KERNELS

Tetrazolium chloride	First perceptible coloration (min)	Coloration equivalent to 30-min staining by 2,3,5-triphenyltetrazolium chloride (min)
2,3,5-Triphenyl	7	30
2,5-Diphenyl-3-(*p*-iodophenyl)	3-4	15
2,3-Di-(*p*-iodophenyl)-5-phenyl	3	10
2-(*p*-Iodophenyl)-3-(*p*-nitrophenyl)-5-phenyl	2	4

Stained sections of sunflower stalk and tumor are shown in Fig. 1. The appearance at 1 hr indicates virtually complete visual specificity in reaction. After 4 hr the appearance of formazan in normal tissue is definitely observable. In color photographs or in actual observation, the contrasts between control and stained sections are more striking. Since these phenomena are based on differential rates of reaction, precise control of test conditions as well as of substituent groups in the compound may be critical in some of the applications of tetrazolium salts.

There were also differences in the actual colors produced. The triphenyl salt upon reduction gave a characteristic pink to carmine color. With the iodo derivative, the red was more pronounced. The diiodo compound gave a more violet-red color, and the color produced by reduction of the iodonitro compound was brownish.

Miscoscopic examination of the stained sections showed considerably less diffusion of color with the three iodine-containing derivatives. More details could be observed in stained parts. This was especially true of the iodo-nitro compound. Because of this property, as well as the rapidity of reduction, this substance may have special value as a biological stain.

Another observation of interest was the photoreducibility of tetrazolium salts by strong reflected sunlight in the presence of some media and the inhibition of such photoreduction in other media. This was first noted in a search for growth inhibitors. Bits of sunflower tumor

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[2] Work supported by the Industrial Science Research Institute of Iowa State College.

[3] Work supported by a research grant from the National Cancer Intsitute, U. S. Public Health Service.

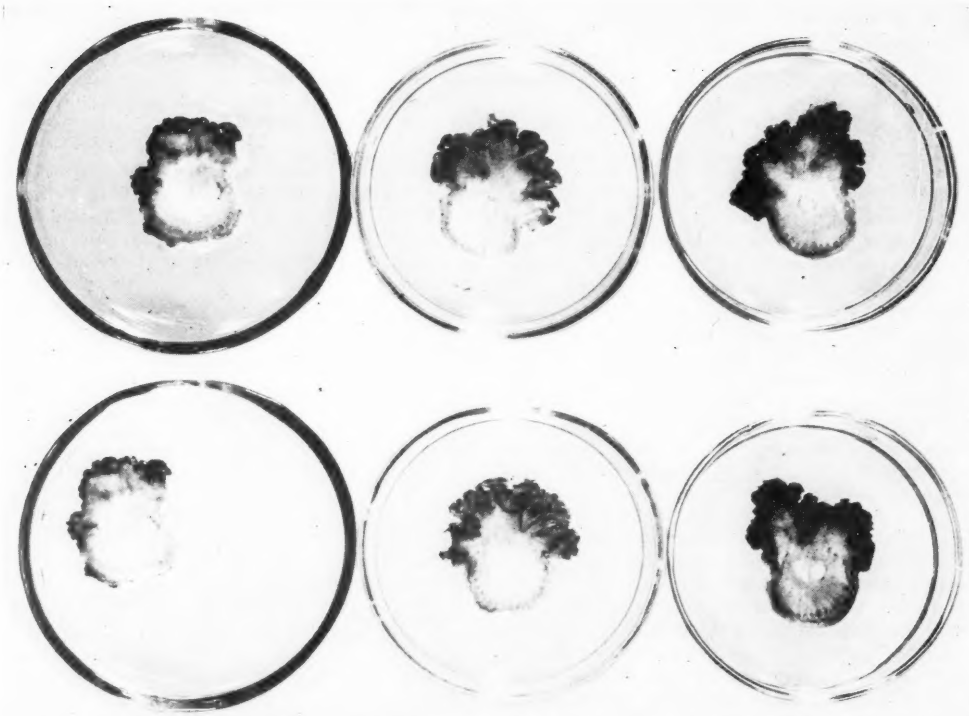

FIG. 1. Photographs of stained sections of sunflower stalk and attached tumor (induced by *Phytomonas tumefaciens*). Sections at the left are controls; those in the middle were stained with tetrazole and those at the right with monoiodotetrazole. The three top sections were stained for 1 hr and the three at the bottom for 4 hr.

tissue were nourished on an agar medium containing 2,3,5-triphenyltetrazolium chloride. The visually colorless medium turned carmine with photographic speed when exposed to sunlight. Similar results were observed in the bacteriological medium of Kuiken *et al.* (*5*);

TABLE 2

EFFECTS OF DIRECT SUNLIGHT AND OF RIBOFLAVIN UPON THE PHOTOREDUCTION OF 2,3,5-TRIPHENYLTETRAZOLIUM CHLORIDE

Solution	Appearance after 5-min exposure
Tetrazolium solution*	Faint pink
Tetrazolium solution + phosphates†	Dark red
Tetrazolium-phosphates + 0.05 μg of riboflavin	Pink
Tetrazolium-phosphates + 0.5 μg of riboflavin	Faint pink
Tetrazolium-phosphates + 5.0 μg of riboflavin	Colorless
Tetrazolium-phosphates + 25 μg of riboflavin	Colorless

* Fifty mg of 2,3,5-triphenyltetrazolium chloride in 5 ml of water.

† Five hundred μg each of KH_2PO_4 and K_2HPO_4 added.

testing various portions of it revealed that the phosphates mixture possessed this property especially (Table 2), and the effect may therefore be one that is particularly pH-sensitive. The presence of small amounts of riboflavin were found to inhibit the reduction.

As a means of determining the approximate photochemical threshold, plastic boxes of four different colors (red, green, yellow, blue) were made. These were placed over the Petri dishes containing the tetrazolium solution to which the phosphate solution was added. At the end of 10 min the solution under the blue box was almost as red as the control which was covered with glass. The solutions under the yellow, green, and red boxes were not appreciably affected. At the end of 1 hr the control and the solution under the blue box were very dark red. The solutions under the green and yellow boxes were uncolored, whereas that under the red box was a very faint pink.

Spectral transmission curves were determined for the plastics used by inserting samples into the light path of a Coleman Model II spectrophotometer. From the curves it was apparent that the threshold must lie near 450 mμ.

Tests made simultaneously on solutions of triphenyltetrazolium chloride, and on the iodo, diiodo, and iodo-

nitro derivatives showed that the triphenyltetrazolium chloride is most subject to photoreduction in sunlight. A solution of the latter compound was definitely pink after 10 min in direct sunlight. At the end of 1 hr, the iodo derivative was barely pink, whereas the other two compounds showed no pink coloration.

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Use of Dyestuffs for Determining the Activity of Proteolytic Enzymes

Benjamin Carroll[1]

Newark Colleges of Rutgers University, Newark, and Department of Chemistry, Columbia University, New York

Numerous investigators (*1*) have shown that native albumin has an affinity for simple dye anions, whether the protein is on the acid or alkaline side of its isoelectric point. This is usually indicated by a spectral change when the protein is added to an aqueous solution of the dye. Pepsin, as well as other proteolytic enzymes, shows practically no combining capacity for these dyes. This fact suggests a new method of determining activity of proteolytic enzymes which may offer advantages.

Klotz (*2*) has shown that common denaturants, such as sodium hydroxide and heat, cause bovine serum albumin to lose its binding ability for anionic dyes. We have found that the action of proteolytic enzymes upon this native protein produces the same effect. Thus a change in the structure of the albumin molecule due to denaturation or fission of its peptide linkages can be detected in the presence of an enzyme. Quantitative activity measurements may be made by estimating the concentration of the native protein in the presence of the proteolytic enzyme as a function of the time, using an empirical curve as is usually done in spectrophotometric analysis. It should be emphasized that this procedure alone will not indicate the state of the protein that has been acted upon by the enzyme. The method is based on measuring the quantity of native protein remaining in solution, whereas the usual activity determination is based on an analysis of the products of hydrolysis.

Fig. 1 shows the effect of a 0.1% pepsin solution upon a 0.2% bovine albumin[2] solution at pH 5.4 in the presence of a constant concentration of the dye, orange I. The extinction is plotted as a function of the wavelength at various time intervals. The cuvettes containing the reaction mixture were kept in the housing of the Beckman quartz spectrophotometer throughout the experiment. No attempt was made to regulate the temperature of the solution, which was about 37° ± 2° C. It will be seen that addition of bovine albumin to the dye causes a depression of about 20% in the absorption maximum, which is in keeping with the data reported by Klotz. Upon addition of crystallized pepsin, the optical density of the reaction mixture in the presence of the dye approaches that for the dye alone.

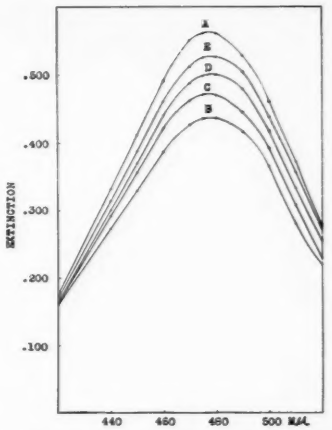

FIG. 1. Effect of 0.1% pepsin on 0.2% albumin in 2.0×10^{-5}M orange I at pH 5.4 (phosphate buffer). A—Dye alone. B—Dye + albumin. C—Dye + albumin + pepsin after 25 min. D—Same as C after 62 min. E—Same as C after 195 min.

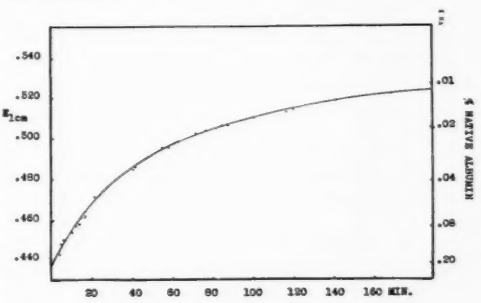

FIG. 2. Optical density at 475 mμ for orange I (2.0×10^{-5}M) in presence of 0.2% albumin and 0.1% pepsin at pH 5.4.

The values of the optical density of the reaction mixture at 475 mμ are plotted as a function of the time in Fig. 2. The values for the concentration scale are on

[1] The interest and suggestions of Prof. A. F. Thomas are gratefully acknowledged.

[2] Crystallized bovine albumin and crystallized pepsin (porcine mucosa) were used in preparation of solutions. These were purchased from the Armour Laboratories, Chicago, Illinois.

the right of Fig. 2. These were obtained from an empirical curve where the optical density was observed at a constant concentration of dye at pH 5.4, while varying the concentration of bovine albumin. The course of the reaction is shown on a semilogarithmic scale in Fig. 3.

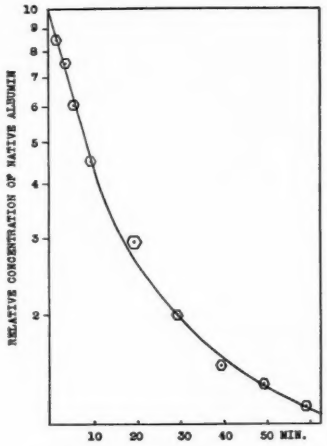

FIG. 3. Fraction of native albumin in presence of 0.1% pepsin at pH 5.4.

It is interesting to note that the half-life of the reaction is about 8 min and that it has gone to 90% completion in 80 min.

The reason for having the concentration of pepsin as high as 0.1%, and the pH at 5.4 instead of the optimum value of pH 2, was to gather information on the nature of enzyme-substrate interaction. Nevertheless, the method is generally the same if conditions of pH and initial concentration of enzyme and substrate are altered. Using the procedure outlined, no particular difficulty was encountered in studying activity of pepsin on albumin at pH 2 when enzyme concentration was one part per billion.

The kinetics of the pepsin-albumin system were studied in considerable detail in 0.01*N* HCl. It has been found that bovine albumin can be kept for several weeks in 0.01*N* HCl without appreciably affecting its binding capacity for simple dye anions. Kinetic experiments involving the variation of the initial concentration of enzyme and substrate showed that these factors had about the same effect as has been established with the usual techniques (*5*) using the formal titration method. An important difference in the activity when determined by the dye method instead of classical methods is that the linear effect of enzyme concentration on the reaction rate can be observed not only at the beginning of the experiment, but even when 50% or more of the native protein has been removed.

Several objections to this method may be raised. One is the possible inaccessibility of substrate to enzyme during the course of the reaction in the presence of the dye. This problem may be removed by simply adding a constant quantity of dye to a given aliquot of the dye-free reaction mixture at various time intervals. This procedure may remove another experimental difficulty, provided the added dye solution is properly buffered to stop the reaction. Thus it is possible to avoid the assumption that the time interval for the albumin and dye to reach equilibrium is inappreciable.

One of the reviewers has criticized this method, stating that "since it is not known what structural changes in the albumin molecule are sufficient to destroy its ability to yield a spectral shift, it is impossible to interpret these kinetic results in terms of denaturation or rate of hydrolysis." Although this may be the state of our knowledge at present, analytical methods do exist which make it possible to determine the extent of both processes and thus interpret the spectral changes quite accurately. A study of the effects of temperature using the dye method indicates an activation energy of about 19,000 calories. This would strongly suggest that the spectral change is due to the breaking of peptide linkages.

Expressing the optical density in terms of concentration of native protein may be an oversimplification. It would be more exact to express results in terms of bound dye anions or available sites on the substrate. The point of complete denaturation (or hydrolysis) and the absence of binding sites on the substrate may not be exactly equivalent. Furthermore, all binding sites on the substrate may not be alike. Until this problem is solved, the use of an empirical curve to obtain concentration values for the substrate appears to be most convenient.

The use of dyes as indicators for following the course of a proteolytic reaction may offer the advantages of increased sensitivity and ease of adaptation of the method to microprocedures. During the course of some work in searching for long range forces (Rothen type [*4*]) in solutions, it became necessary to determine the effect of pepsin on bovine albumin, which had an initial concentration of 1 ppm. The dye method was found suitable for handling this problem.

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Comments and Communications

Extension of Political Domination beyond Soviet Genetics

The widely discussed antigenetics campaign, linked with the name of Trofim Lysenko, has raised in the mind of many a Western scientist questions as to the possible implications of Lysenko's crusade for other branches of science. It is the aim of this paper to provide some information on the reverberations of the genetics controversy in physiology and biochemistry.

It has been obvious from the start that more than genetics was at stake. Lysenko presented the controversy as just one facet of the struggle between the "materialist" and the "idealist" outlook in science, sure to affect the foundations of nearly all branches of biology (Lysenko, T. *The science of biology today.* New York: International Publishers, 1948. P. 16.). In the session of the council of the Academy of Sciences of the USSR held August 24–26, 1948, action was taken against the physiologist Orbeli, president of the biology section of the Academy of Sciences, as well as against Shmalhausen, director of the Institute of Evolutionary Morphology, and the cytologist Dubinin. The section of biological sciences was directed to review the matter of scientific personnel and publication facilities, and to look after the Michurinist genetics. The section of history and philosophy was to devote attention to the generalization and theoretical interpretation of the achievements of Michurin and his disciples (Levy, J. *Science and Soc.*, 1948–49, 13, 61).

But the steam-roller of the Lysenko "revolution" did not stop there. At the session of the Academy of Medical Sciences it was stressed that medicine should make use of the conquests of biology produced by the Michurin doctrine (Levy, J. *Op. cit.* P. 62). Scientific journals in basic medical sciences hastened to note Lysenko's "discoveries" and greeted the event as opening a new epoch in Soviet biology. The editors beat their breasts loudly in ostentatious repentance, combined with a paradoxical air of "We have been saying the same thing all along." The editorial in the November–December, 1948, issue of the *Sechenov Journal of Physiology*, established by I. P. Pavlov in 1917 and published by the Academy of Sciences of the USSR, may serve as a good example (Editorial. *Sechenov J. Physiol. U.S.S.R.*, 34, 661–664). The fact that the journal has been maintaining high scientific standards provides an even sharper contrast to the level of the editorial.

The editors acknowledged with a flagellant's satisfaction that the discussions at the meeting of the Agricultural Academy (*The situation in biological science: Proceedings of the Lenin Academy of Agricultural Sciences of the U.S.S.R., July 31–August 6, 1948. Complete stenographic report.* New York: International Publishers, 1949.) have revealed a series of errors committed by the Soviet biologists. These errors delayed the development of biological sciences (and, by inference, constitute sabotage of a speedy realization of the socialist commonwealth). These principles of "creative Darwinism," as the Lysenko dogma is called, must be incorporated without delay into all biological disciplines.

Until recently an erroneous idea was held widely—continued the editorial—the idea that defeat of Weismann-Morgan genetics does not affect those biological disciplines which are not directly concerned with the problem of inheritance, such as experimental physiology, which investigates the concrete mechanisms underlying the function of the animal and human organism. In Soviet physiological textbooks and physiological journals one does not encounter the term *gene* or *chromosome.* However, say the editors, it would be a sign of narrowness if physiology were to remain aloof and fail to be fertilized by the ideas of the Michurin-Lysenko school of thought. Such a tendency would indicate a lack of correct "orientation."

The editors concede that physiologists have been concerned with developmental aspects of organic functions. But, they ask, did the physiologists even phrase the question about the *leading* principle of developmental physiology? No! They did not recognize the full significance of the work of Michurin and his follower, Lysenko. They failed, say the editors, to relate the experience of the great transmutator of plants, Michurin, to their investigations on the evolution of functions of animal organisms.

The editorial attempts to minimize the number of Soviet biologists who professed adherence to "Western" genetics. And yet in the next sentence the editors go on, penitently, to admit that until the August, 1948, session of the Agricultural Academy, "All of us failed to appreciate fully the reactionary essence of idealistic tendencies in the theory of inheritance, widely disseminated abroad and having penetrated, unfortunately, into our country." "We have failed to appreciate these facts and that was the reason we took no part in the fight" (Editorial. *Sechenov J. Physiol. U.S.S.R.*, 34, 362).

Having torn their robes in sadness that they were not, after all, such good Marxists as they had thought, and having sprinkled ashes thick on their weary crania, the editors tried to blow up a few straws to clutch. They noted that I. P. Pavlov in his investigations on conditioned reflexes had demonstrated the interdependence between the organism and its environment, and had examined physiological mechanisms by which functional bonds are acquired in the ontogenesis of the organism. And they cited the studies by Pavlov's pupil, K. M. Bykov, on the relations between the cerebral cortex and inner organs, and the work of other laboratories, devoted to the study of the influence of the environment on the animal organism, particularly on its higher nervous activity.

Furthermore, the editors credit Pavlov with having considered the problems of inheritance in reference to

the nervous system and having started experimental work in that direction. He died before he was able to complete them. We are informed that in Pavlov's institute for the experimental genetics of higher nervous activity, studies had been initiated before the war and are actively pursued now, directed toward producing inheritable changes resulting from the action of factors of the external environment.

In a way, this is old stuff, argue the editors. Orbeli, editor-in-chief of the journal, is said to have put forth the concept of the inheritance of acquired characteristics as a principle of the evolution of the nervous system a long time ago. A passage is cited from a 1923 paper on "Mechanisms of the Origin of Spino-cerebral Coordinations":

> Investigations on conditioned reflexes reveal the way of the functional evolution of the nervous system. The ready-made coordinating mechanism with which we are born was created in the course of thousands of years according to the same basic laws by which new coordinating bonds are created in the course of weeks, sometimes days and hours, in the course of an individual life.

The editors themselves feel that their arguments are weak and the penitent mood dominates the next move. It is true, they go on, that Soviet physiologists have not promulgated anti-Michurinist doctrines, but they have not declared specifically that Morganist principles are basically foreign to them. The Soviet physiology, based on the work of Sechenov, Pavlov, and Vedenskij, cannot but be materialistic. The physiologists must scrupulously scrutinize their ideological direction and must orient the development of physiology in such a way as to exclude any possibility of contamination with ideological tendencies foreign to a materialistic philosophy. Attempts at a revision of the materialistic bases of Soviet physiology, encountered in the work of some of the Soviet physiologists, must be eradicated. But that is not enough. Soviet physiology must be constructed on the principles of the great progressive biological theory of Michurinism!

The biochemists, in their turn (Editorial. *Biokhimiya*, 1948, **13**, 393–396.), rushed in to praise the Lysenko revolution as "a very important landmark in the development of all science concerning the living world." Mr. Lysenko is congratulated on having

> . . . revealed in a profound manner the ideological struggle in biology and showed the complete fruitlessness of the reactionary idealistic teachings of Weissmann-Mendel-Morgan. . . . At the same time he gave clear testimony to the vitality and power of progressive Michurinist science. The firm foundation of the dialectic-materialistic world outlook and the unbreakable bond with the urgent needs of the national economy characterize the Michurinist direction in science. Its significance thus far transcends the limits of biology and extends to the natural sciences as a whole.

This applies, say the editors, in full measure to biochemistry, which "cannot find the correct lines of development except as they are pointed out by the progressive Michurinist science." In the past, the representatives of biochemistry have not repulsed, as they should have done, the attempts by Morganist-Mendelists

> . . . to appropriate the achievements of biochemistry for the purpose of hiding their idealistic outlook by pseudomaterialistic formulations. More than that, we meet with direct acknowledgement of these pseudoscientific postulates, with thoughtless and uncritical use of concepts and ideas which are the bases of the chromosomal theory of inheritance.

Still in 1948 there were men, like S. I. Alikhanyan, who expressed publicly the belief that significant progress in genetics will result from the biochemical study of the action of the genes. Y. O. Parnas, V. L. Ryzhkov, and V. I. Tovarnitskij formulated theories not distinguishable from the bourgeois genetics of Beadle. Something had to be done about this state of affairs.

> The task of our scientific press, of all media of scientific propaganda, and of the actual activities of our research institutions is to combat relentlessly and with determination every kind of penetration into biochemistry of foreign, idealistic views and at the same time to draw the attention of the broad masses of biochemical research workers to the truly urgent and realistic objectives of biochemical research. . . . to pass quickly from a contemplative attitude [of the purely analytical, descriptive research] to an active intervention in the chemistry of living things.
>
> "Know how to change the metabolism of the living body and you shall change its heredity," such is the objective set by T. D. Lysenko for Soviet biology, and directly addressed to biochemical research.

Other disciplines, in their turn, are drawn into the maelstrom: neuropsychiatry (Grashchenkov, N. I. *Nevropatol. Psikhiatr.*, 1948, No. 5, 3–16), psychology (Bauer, R. A. *Amer. Psychologist*, 1949, **4**, 418), even education and law.

One may ask: Why was a technical point, important but limited in scope, made a battlefield? Because *it became not a theoretical but an "ideological" problem.* It was accepted as a foregone conclusion that "Weismann-Morgan genetics" leads necessarily and logically to racism, and the conclusion was drawn that Western genetics represents vicious "idealistic" ideology. The fact that Western scientists sharply criticized the Nazi prostitution of genetics is nowhere mentioned. To arms, the cry resounds, here you see clearly the demonstration of one of the basic tenets of Marxism—namely, that all science, including biology, constitutes an area of struggle between materialistic and idealistic philosophy which reflects the struggle between progressive and reactionary forces of humanity. The case of genetics—go on the Soviet dialecticians—demonstrates the deep truth of Leninist-Stalinist teaching that science must retain a "party-character" (*partijnost nauki*); departure from this principle leads to the support of the enemy camp.

These are profoundly disturbing developments. The antithesis in political systems and the tensions resulting from the struggle between the Eastern and the Western power blocs for supremacy are beyond the hope of real reconciliation. In the past, science—at least the natural sciences—provided a common meeting ground. Soviet scientists were, on the whole, well acquainted with the work done abroad. Their bibliographical references in scientific journals, such as the physiological journal which printed the infamous editorial, demonstrates that the Soviet scientists were actually less provincial in their reading than some of their American colleagues.

The victory of Lysenko's irrationalism and chauvinism, reliance on the backing of the Party in a scientific con-

troversy, the xenophobic attitude toward "foreign" scientific theories—all of these increase the gulf between East and West. At a time when the equilibrium of peace is more than precarious, the added heat, from which no light can be expected to come, dangerously increases the chances of an explosion.

To estimate the real significance of these events for the development of Soviet biology and medicine is not an easy task. So far, the actual content of the journals has not changed. Will the storm affect only the political teapot, and does it represent a phenomenon which must be explained primarily in terms of internal power politics? It may be noted that Lysenko directed his campaign, started as far back as 1935, against Nikolai I. Vavilov, whom he finally (in 1939) replaced as president of the Lenin All-Union Academy of Agriculture. This may be a part of the story but is certainly not all of it.

The climate of opinion, the "Zeitgeist" characterized by nationalism, curiously intertwined with communist ideology, provided both stimulus and receptive ground for the flowering of Lysenkoism. Lysenko's slipshod methods were repeatedly criticized. C. D. Darlington. (*J. Hered.*, 1947, **38**, 145) pointed out that in "proving" the inheritance of environmental effects Lysenko began the experiments with a mixed stock, omitting to use proper controls and repudiating statistical tests. This laxity in scientific standards, which seems to heap gold and honor on Lysenko, is likely to be contagious in the Soviet Union.

Competent geneticists are in agreement that Lysenko's views would never be discussed, had they not become of political importance in the Soviet Union: "Lysenko displays an astonishing ignorance of the real nature of the views he is attacking. Several of his own purported results are at variance with the general experience—work carried on over many years, with many kinds of organisms, in many parts of the world" (Sturtevant, A. H. Personal communication, 1949). This will not prevent satellite minds, not necessarily residing in satellite countries, from swallowing eagerly, the "new line," hook and sinker. What would Descartes say to his compatriot Marcel Prenant. (*Science and Soc.*, 1948–49, **13**, 50–54), who defends the Soviet Michurinists by arguing that "In a socialist country menaced by aggression, as is the U.S.S.R. today, biologists who are aware of their responsibilities *have more urgent things to do than to touch up the details of theory*"? (Italics mine.)

The implications of the genetics controversy reach not only beyond the field of genetics (Huxley, J. *Heredity east and west: Lysenko and world science.* New York: Henry Schuman, 1949) but also beyond the geographical frontier of the USSR. Like Stahl's theory of phlogiston, the heat substance lost in the process of burning, the exhumed theory of the inheritance of acquired characteristics, reinforced by the spirit of scientific dogmatism, may prove to be a real handicap to the progress of scientific biology in a large part of the world.

JOSEF BROŽEK

Laboratory of Physiological Hygiene
University of Minnesota, Minneapolis

Atomic Energy and the New Dictionaries

It is pertinent to the current evaluation of *The American College Dictionary* and *Webster's New Collegiate Dictionary* to report that an examination of them for words used in nuclear physics and chemistry, especially those concerned with the development of atomic energy, shows *WNCD* superior both in number of entries and informativeness of definition. One hundred twenty-four expressions were looked up in both dictionaries. The entry was counted only if the expression was defined in the nuclear sense. And the entry was still counted if if gave no definition at all but referred to another entry defined in the nuclear sense. Of the 124 expressions, 83 were not found in either dictionary, 23 were found in both, 15 were found in *WNCD* alone, and 3 in *The ACD* alone. Of the 83 not found in either dictionary, most are too recent, technical, or transitory for inclusion, but a few omissions seem odd even when time is considered. *Reactor*, for example, does not appear in either dictionary; nor do *atom smasher, electrostatic generator, Mev, particle* and *particle accelerator, radioactive isotope*, and *triton*. More surprising than the omission of *reactor* is the omission of *uptake*, which has long been in use generally among biologists to mean to absorb and retain, and is now appearing in nuclear writings: "The uptake of radioactivity by the land and water organisms. . . ." (U. S. Atomic Energy Commission. *Atomic Energy Development 1947–1948*, Washington, D. C., p. 93).

The 15 expressions contained in *WNCD* but not in *The ACD* are *fission* (*The ACD* does not have the nuclear application), *meson* (*The ACD* has *mesotron* but not *meson*), *metastable state, microcurie* (under *micro*), *moderator, nuclear energy, nucleon, nucleonics, penetrometer, photodisintegration, photoelectron, radioelement, reaction* (nuclear), *servo* (*system*), and *tracer* (*radioactive*). The three in *The ACD* but not in *WNCD* are *classify* (in the sense of to put into a secret class), *radioactive series*, and *cloud chamber*—this last is a curious oversight by *WNCD*. The fact that *The ACD* (copyright 1947) is some two years older than *WNCD* (copyright 1949) may account in part for the larger number of nuclear entries in the latter; on the other hand, according to advertisements *The ACD* totally has more entries than *WNCD*, 132,000 to 125,000. But what accounts for the superiority of *WNCD* in the definitions of words common to both dictionaries seems to be simply greater care plus larger space.

The definitions of the 23 expressions that both dictionaries contain were compared for informativeness—a combination of accuracy, quantity, precision, and clarity. Neither was better than the other in nine words, *WNCD* was better in 12, and *The ACD* was better in two. The 12 terms in the definitions of which I found *WNCD* superior are *betatron, chain reaction, curie, Geiger counter, half-life, isotope, meson-mesotron, pair production, photoelectric, pile, positron*, and *radioactive-radioactivity*. *The ACD* two are *atomic bomb* and *dosimeter*. Three examples will show what I mean by a better definition—in the first one *The ACD* is better; in the second and third, *WNCD*.

(1) atomic bomb

The ACD: 1. A bomb whose potency is derived from nuclear fission of atoms of fissionable material, with consequent conversion of part of their mass into energy. 2. A bomb whose explosive force comes from a chain reaction based on nuclear fission in U-235 or in plutonium. It was first used militarily on Hiroshima, Japan (August 6, 1945). The explosion of such a bomb is extremely violent and is attended by great heat, a brilliant light, and strong gamma-ray radiation.

WNCD: A bomb whose violent explosive power is due to the sudden release of atomic energy. The release results from the splitting, or fission, of heavy nuclei (plutonium, uranium) by bombardment with particles (neutrons).

(2) Geiger counter

The ACD: An instrument for detecting and counting ionizing particles, consisting of a tube which conducts electricity when the gas within is ionized by such a particle. It is used in measuring the degree of radio-activity in an area left by the explosion of an atom bomb, in investigations of cosmic rays, etc.

WNCD: [After Hans *Geiger* (b. 1882), German physicist.] *Physics.* A thin-walled metallic cylindrical tube with a needle-like electrode projecting within, which detects the passage through its walls of every ionizing particle, such as a cosmic-ray particle, by the momentary current set up on ionization of the contained gas. A similar sensitive counting tube, the *Geiger-Müller counter* . . . containing a slender axial wire, is used for detecting radioactivity and making quantitative measurements.

(3) pile

The ACD: 7. *Nuclear Physics.* A latticework of uranium and various moderating substances used to produce plutonium in the original harnessing of atomic energy. It is essentially a means of controlling the nuclear chain reaction.

WNCD: 5. *Physics & Chem.* An arrangement of fissionable material, with a moderator (as carbon or heavy water, for slowing down neutrons) and regulating devices, designed for producing and controlling a chain reaction, as for making plutonium from uranium or producing atomic energy, by the action of neutrons;—called specif. *atomic pile, chain-reacting pile.*

The ACD usually gives the shorter definition, but the longer definition in *WNCD* I found to be more informative without any sacrifice of clearness.

E. N. LOCKARD

Chicago City Junior College
Argonne National Laboratory

Scientific Book Register

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Trilinear Chart of Nuclear Species. William H. Sullivan. London: Chapman & Hall; New York: John Wiley, 1949. Illustrated. $2.50.

Biologie der Goethezeit. Adolf Meyer-Abich, Ed. Stuttgart, Germany: Hippokrates-Verlag Marquardt; Waltham, Mass.: Chronica Botanica, 1949. 302 pp. $5.50.

Topology of Manifolds. Raymond Louis Wilder. New York 27: American Mathematical Society, 1949. 402 pp. $7.00.

Quinidine in Disorders of the Heart. Harry Gold. New York: Paul B. Hoeber, Harper, 1950. 115 pp. $2.00.

Some Early Tools of American Science: An Account of the Early Scientific Instruments and Mineralogical and Biological Collections in Harvard University. I. Bernard Cohen. Cambridge, Mass.: Harvard Univ. Press, 1950. 201 pp. $4.75.

NEWS and Notes

George B. Pegram, 73-year-old vice president of Columbia University, will retire June 30. He has been appointed special advisor to Columbia's president for a one-year term beginning July 1, and will also serve as scientific and educational consultant at the Oak Ridge Institute of Nuclear Studies during the coming academic year.

C. O. Dunbar, director of the Peabody Museum of Natural History at Yale University, **R. L. Flint,** Yale professor of geology, **L. C. Graton,** professor of geology, and **A. S. Romer,** professor of zoology, both of Harvard University, were recently elected members of the Geological Society of London.

Cyrus C. Sturgis, professor of medicine, University of Michigan Medical School, and director of the Thomas Henry Simpson Memorial Institute for Medical Research, will deliver the ninth Edwin R. Kretschmer Memorial Lecture of the Institute of Medicine of Chicago on Friday evening, April 28, at the Palmer House. His subject will be "An Evaluation of the Nature, Treatment, and Prognosis of Leukemia."

John S. Poe, formerly of Columbia University College of Physicians and Surgeons, has been appointed professor of neuropsychiatry and head of the department at the University of Arkansas School of Medicine, effective May 1. **H. Lee Hall** has been appointed associate professor of neuropsychiatry, effective July 1. Dr. Hall was formerly associated with the Long Island College of Medicine.

Arthur F. Sievers retired March 31 from the U. S. Department of Agriculture after 43 years of service devoted to research on the culture and analysis of plants producing drugs, poisons, insecticides, essential and fixed oils, perfumes, and related products. For the past 25 years he has had the major responsibility for these investigations, with headquarters for the past ten years at Plant Industry Station, Beltsville, Maryland.

Darol K. Froman has been named technical associate director of the Los Alamos Scientific Laboratory to replace **John H. Manley,** who has resigned to devote more time to research. Dr. Froman has been a member of the staff since 1943, and was scientific director of the atom bomb tests at Eniwetok in 1948.

Hermann I. Schlesinger, professor emeritus of chemistry of the University of Chicago, is delivering Cornell University's George Fisher Baker nonresident lectures, which began April 4 and will continue for six weeks. The lecture series is entitled "Recent Developments in the Hydrogen Compounds of the Lighter Elements."

Joseph Bernhardt Rosenbach, a member of the Carnegie Institute of Technology faculty for three decades, has been named head of the Department of Mathematics. Dr. Rosenbach has been assistant head of the department since 1946.

Samuel Soskin has resigned as medical director of Michael Reese Hospital in Chicago, in order to spend full time on his duties as director of the Medical Research Institute, and as dean of the Michael Reese Hospital Postgraduate School.

Joseph Anderson has joined the staff of the Laboratory of Physiological Hygiene, University of Minnesota, as assistant professor in the School of Public Health. He was formerly in the Department of Physiology at the University of Rochester.

Visitors to U. S.

Manimo Cimino, astronomer with the Rome Observatory, recently visited the Palomar and Mt. Wilson Observatories.

James G. Morrow, chief metallurgist, The Steel Company of Canada, Ltd., Hamilton, Ontario; **J. G. Reynolds,** senior research chemist, Thornton Research Center of the Shell Refining and Marketing Company, Thornton, England; and **Balth Van Der Pohl,** director, and **Leslie Hayes,** vice director of the International Radio Consultative Committee of Switzerland, were recent visitors at the National Bureau of Standards.

F. H. Bentley, professor of surgery, Newcastle-upon-Tyne, University of Durham, England, was a recent lecturer at the Mayo Foundation clinic, in Rochester, Minnesota.

Grants and Awards

A $30,000 grant by the **David P. Wohl Foundation** of St. Louis has been made to the St. Louis University School of Medicine to establish the Wohl Memorial Institute of Experimental Surgery. The Firmin, Desloge, and St. Mary's hospitals will also utilize the institute, which will provide preoperative and postoperative wards, anesthetic, sterilizing, and operating rooms, and a diet kitchen.

The 1950 Carl Neuberg Medal was awarded to Jesse P. Greenstein, chief of the Biochemistry Section of the National Cancer Institute, U. S. Public Health Service, by the Association of European Chemists and Pharmacists of New York, on March 14. Dr. Greenstein was cited for his contributions to chemistry and biochemistry, particularly for his work on enzymatic behavior of normal and neoplastic tissue, demonstration of dehydropeptidase activity in protein metabolism, and development of an enzymatic method for obtaining optically pure amino acids.

Summer Programs

The fourth summer session of the Gulf Coast Research Laboratory will be held at Ocean Springs, Mississippi, from June 6 through August 25. Laboratory courses will be offered for both graduate and undergraduate students in botany, invertebrate zoology, marine sedimentation, ichthyology, chemistry, endocrinology, parasitology, techniques in biology for high school teachers, and science for elementary teachers, and

research facilities will be available. Students from other states will be accepted on a regional basis, without out-of-state tuition charge. Further information may be obtained from Dr. R. L. Caylor, Delta State Teachers College, Cleveland, Mississippi.

A summer school on the **physics and chemistry of free radicals** will be held in the Department of Physical Chemistry, University of Cambridge, England, August 19–26. Lecture courses and demonstrations will be given on the structure, spectroscopy, and mass spectroscopy of free radicals; free radicals produced by light and nuclear radiation, and their reactions; the role of free radicals in combustion and polymerization; and free radical reactions in solutions. Further details and application forms may be obtained from the Secretary of the Summer School, Department of Physical Chemistry, Free School Lane, Cambridge.

The Yale Summer School of Alcohol Studies will hold its eighth annual session at the university July 8–August 4. The program, which includes 55 lectures, informal group meetings, visits to the laboratory and clinics, and consultation with staff members, will be under the direction of Elvin M. Jellinek, research associate in applied physiology. Emphasis will be placed upon problems of alcoholism in industry and a special workshop will be provided for those engaged in personnel work. Part or whole scholarships are awarded annually by the school to qualified persons. All correspondence concerning enrollment should be addressed to the Summer School of Alcohol Studies, Laboratory of Applied Physiology, Yale University, 52 Hillhouse Avenue, New Haven, Connecticut.

The University of Connecticut announces that an eight-week conservation tour of the U. S., covering 12,000 miles, will be conducted during the summer of 1951. The trip will be made by bus with traveling kitchen over a southern route to the West Coast, north to Washington, and back to Connecticut by a northern route, permitting firsthand study of examples of our national resources. Enrollment will be limited to 20, and applications will be considered in order of receipt. The cost of the tour is estimated at $400, which will cover transportation, food, tuition, and necessary incidentals. The exact date of the tour has not yet been determined, but enrollment must be completed by *March 1, 1951*. Further information may be obtained from Dr. Raymond Kienholz, Coordinator, University of Connecticut, Storrs.

The University of Michigan will hold three symposia, from June 26 to August 18, as part of its summer session. Visiting lecturers from other universities and from industrial and government laboratories will take part. The Department of Electrical Engineering will sponsor a **specialized electronics symposium,** with A. H. W. Beck, of Standard Telephones and Cables, Ltd., Ilminster, England, as one of the visiting lecturers. Information about this symposium may be obtained from Prof. W. G. Dow, Director of the 1950 Summer Electronics Symposium, Department of Electrical Engineering, University of Michigan, Ann Arbor. The Department of Physics will offer **a symposium on theoretical physics,** considering cosmic ray principles, high energy physics, theory of the solid state, and general field theories. Freeman Dyson, of the University of Birmingham, England, will lecture. Sydney Goldstein of the University of Manchester, England, will lecture at the **symposium on fluid mechanics,** sponsored by the Department of Engineering Mechanics. Information concerning these two symposia may be obtained from the Department of Physics, and from the Department of Engineering Mechanics, respectively.

Meetings and Elections

The first midwestern conference on fluid dynamics and a meeting of the **Fluid Dynamics Division of the American Physical Society** will be held at the University of Illinois, May 12 and 13. The university's new $1,602,000 mechanical engineering building will be dedicated at the same time.

The American Institute of Chemical Engineers has scheduled two symposia on new engineering processes for the Boston regional meeting, to be held May 28–31 at Swampscott, Massachusetts. Dudley Thompson, of Virginia Polytechnic Institute, will conduct the symposium on ultrasonics, which will include papers on chemical, physical, and colloidal effects produced by ultrasonics, and industrial utilization of ultrasonic energy. The symposium on fluidization will be supervised by E. R. Gilliland of Massachusetts Institute of Technology, and will include papers on diffusion rates in porous solids, and results of flow of gas and solids in a commercial catalytic cracking unit. A general technical session will also be held. Advance registration and inquiries should be sent to J. J. Healy, Jr., Monsanto Chemical Company, Everett, Massachusetts.

The Springfield chapter of the AAAS will meet at Smith College on April 28. The meeting will be preceded by a formal dinner at 6:30. At 8:30, Francis O. Schmitt, of Massachusetts Institute of Technology, will speak on "Some Aspects of Molecular Biology." Dinner reservations of $1.75 should be sent to Prof. N. M. Mohler, Lilly Physics Laboratory, Smith College, Northampton, Massachusetts.

More than 300 papers, covering all phases of medical and surgical progress, will be presented at the 99th annual meeting of the **American Medical Association,** to be held June 26–30 in San Francisco's Civic Center. General scientific meetings will be held on the first two days of the convention. Sectional groups will meet on the next three days. The section programs will deal with anesthesiology, dermatology, and syphilology, diseases of the chest, experimental medicine and therapeutics, gastroenterology and proctology, internal medicine laryngology, otology, rhinology, physical medicine and rehabilitation, military medicine and surgery, allergy, nervous and mental diseases, obstetrics and gynecology, ophthalmology, orthopedic surgery, pathology and physiology, pediatrics, preventive and industrial medicine,

public health, radiology, general and abdominal surgery, and urology.

More than 280 exhibitors will stage a technical display at the Civic Auditorium during the week. Surgical operations performed in one of the local hospitals will be transmitted in color to 20 receivers in Masonic Hall over a closed television circuit.

The installation of Elmer L. Henderson, of Louisville, Kentucky, to succeed Ernest E. Irons, of Chicago, will take place on the evening of June 27. The annual award for distinguished service to the medical profession will be made the same evening.

The London Conference on Optical Instruments will be held July 19–26 at the Imperial College of Science and Technology in South Kensington, in concurrence with the official sessions of the International Optical Commission, which begins July 17 at the Royal Society headquarters at Burlington House. There will be symposia on reflecting microscopes, phase-contrast microscopes, gratings and grating instruments, reflecting telescopes, and spectrophotometers. Joint discussions with the commission will deal with diffraction in optical instruments and new optical materials. U. S. scientists who will speak at the conference are Stanley S. Ballard, of Tufts College, Carl Bausch, president of Bausch and Lomb Optical Company, David S. Grey, of the Polaroid Corporation, and Rudolf Kingslake, of the Eastman Kodak Company .

The Northeastern District of the American Institute of Electrical Engineers will hold a meeting in Providence, Rhode Island, April 26–28. Advance registration should be made with H. C. Rankin, Chairman, Registration Committee, Narragansett Electric Company, 49 Westminster Street, Providence. A fee of $2 is required for members and $3 for nonmembers.

The Plastics Committee of the Massachusetts Institute of Technology will hold a **summer conference on the mechanical properties of plastics,** in research and engineering applications, June 20–22. Emphasis will be placed on theories of fiscoelastic behavior and on experimental work being done to determine the fundamental mechanical behavior of high polymers. Further information may be obtained from Prof. Albert G. H. Dietz, Room 5-209, MIT, Cambridge.

The South Carolina Academy of Science will hold its annual meeting at Winthrop College, Rock Hill, South Carolina, on April 22, with the **South Carolina Section of the American Chemical Society.** Over 30 papers and several exhibits and demonstrations have been scheduled. Papers will be presented by those competing for the Jefferson Award, offered by Phipps and Bird, of Richmond, Virginia, for original research.

Deaths

Sir Norman Haworth died in Birmingham, England, March 19, on the eve of his 67th birthday. He was professor of chemistry at Birmingham University from 1925 until his retirement last year. In 1937 he shared the Nobel Prize in chemistry with Paul Karrer for his work on vitamins and carbohydrates. Sir Norman was an authority on the chemical composition of sugar and his textbook *The Construction of Sugar,* published in 1929, is well known to organic chemists.

Oskar Baudisch, 68, director of research at New York State Institute for Balneology and Hydrotherapy since 1934, died March 28 by accidental drowning at La Jolla, California, where he had been working on a research project on trace elements in the sea for the Scripps Institution of Oceanography. Dr. Baudisch was well known for his development of the analytical reagent cupferron and other organic precipitants for study of natural water.

Merle Randall, professor emeritus of chemistry of the University of California, Berkeley, died March 17 at the age of 62. Dr. Randall joined the staff of the university in 1912, became professor of chemistry in 1927, and professor emeritus in 1944. He was engaged in research on heavy water before World War II.

Percy N. Annand, chief of the Bureau of Entomology and Plant Quarantine of the U. S. Department of Agriculture, died March 29, following a long illness. He was 51. Dr. Annand was an authority on insects and insect control, and many of the recent developments in this area, including use of DDT, aerosols, and dispersal of liquid insecticides from airplanes, were made under his direction.

Adolph Meyer, 83, professor emeritus of psychiatry at Johns Hopkins University Medical School, died March 17 at his home in Baltimore. Dr. Meyer, who was specially interested in the application of psychiatry to penology, was head of the Phipps Psychiatric Clinic at the university, from its founding in 1912 until he retired in 1941.

George F. Gebhardt, 76, former director of the Department of Mechanical Engineering at Illinois Institute of Technology, died March 22 at his home in Miami, Florida. He was a member of the faculty of Armour Institute of Technology (now Illinois Institute of Technology) from 1898 until his retirement in 1934.

The Freud Memorial Committee of the Institute of Psychoanalysis in London is planning publication of translations of Freud's complete works dealing with psychoanalysis, psychology, and related subjects. The material will be arranged in chronological order in 23 volumes, with a separate index volume. The committee offers subscribers a special rate of $120 for the set, and each volume will be distributed as it is published, beginning in 1950. It is expected that the complete translated edition will be ready for distribution in 1956. Information may be obtained from the American Psychoanalytic Association, 245 East 82nd Street, New York City.

The World Health Organization has announced recent agreement with Czechoslovakia, Denmark, and Poland, for the establishment of medical training centers where courses will be given on an international

basis. A center for training in anesthesiology will be set up in Copenhagen, and a similar one in Prague, to provide facilities for study of new techniques, under WHO's fellowship program. Two training centers will be set up in Poland—one at Wroclaw, in biochemistry, and one in venereal disease control at Warsaw. WHO will cooperate with the national health aoministrations and medical faculties of the countries in establishing a curricula and providing equipment, in addition to aiding with fellowships.

The Senate-House conference committee to resolve the differences between the Senate and House versions of the **National Science Foundation bill** met on April 4 and 5, and then adjourned to reconvene on April 19, after the expiration of the Easter recess.

The conference committee accepted the $15,000,000 ceiling of the House bill, but spent most of its two meetings on the loyalty provisions. They agreed to drop the Smith and Flood amendments and to write a substitute. It is anticipated that the requirement of loyalty investigations will be limited to employees, contractors, and scholarship and fellowship holders who have access to information affecting the national security. All scholarship and fellowship holders, however, will be required to sign an oath of allegiance and affidavit of loyalty. The exact wording of the loyalty provisions has not yet been settled and can of course be changed when the conference committee meets again on April 19.

English abstracts of Russian books and articles in astronomy and astrophysics are made available through the medium of the *Astronomical Newsletter*, which is issued at irregular intervals from the Harvard College Observatory. The *Newsletter* was started during the war by Bart J. Bok of the observatory, under the auspices of the American Astronomical Society. The wartime series of 36 *Newsletters* was devoted primarily to those articles which, because of wartime conditions, were not widely distributed. After the Russian publications adopted the practice of printing only in the Russian language, the society requested Dr. Bok to renew the *Newsletter* and use it entirely to cover as much of the Russian literature as could be found in this country.

Margaret Olmsted of the Harvard Observatory has undertaken the responsibility for issuing the *Newsletters* of astronomical literature, prepared by the committee for distribution. Those who now participate in the work of abstracting include A. N. Vyssotsky, S. Gaposchkin, Z. Kopal, L. Jacchia, and O. Struve, who also acts as the coordinator and editor of the group. To date, 12 issues have appeared, averaging approximately 10 pages per issue. The subscription price ($3 for about 50 pages) should be sent to Miss Olmsted, Harvard College Observatory, Cambridge, Massachusetts.

A clinical section on general medicine and experimental therapeutics has been established as part of the research program of the National Heart Institute of the U. S. Public Health Service. Luther L. Terry, chief of the Medical Service, U. S. Marine Hospital in Baltimore, will head the new section, which will function as a clinic at the Marine Hospital until the opening of the new clinical center of the National Institutes of Health in Bethesda, Maryland, in 1952. The section will emphasize study of the problems of hypertension and methods for its treatment.

The Registry of Rare Chemicals, 35 West 33rd Street, Chicago, Illinois, lists the following wanted chemicals: cesium oxide, cadmium carbide, germanous fluoride, ß-fluoropropionic acid, sodium cyclohexanesulfonate, 3-aminophenol, carbamyl bromide, 4-methyl-1,3-dioxane, glyceryl caproate 2-phenyl-*n*-propyl amine, 1-(2,4-dinitrophenyl) semicarbazide, di-*n*-butyl formal, α-cyclogeranic acid, β-cyclogeranic acid, 2-(D-pantoylamino) ethylsulfono-4-chloroanilide, 1,3-diphosphoglyceric acid, 5,6-dimethylbenzimidazole, 1-methyl-2-mercaptoimidazole, trypiticase, and uropepsin.

A certifying board, **The American Board of Nutrition,** to establish standards of qualifications for specialists in human nutrition, and to certify as such persons who comply with the standards, has been organized. Those concerned with the establishment of the board included representatives from the American Institute of Nutrition, American Medical Association, American Public Health Association, American Society of Biological Chemists, Inc., and Association of American Medical Colleges. Present members are Otto A. Bessey, C. A. Elvehjem, Wendell R. Griffith, C. G. King, L. A. Maynard, Frederick J. Stare, and John B. Youmans. Qualified candidates will be considered for certification without examination until *June 30, 1951*. Prescribed forms for applications, and further information may be obtained from the office of the Secretary-Treasurer, Otto A. Bessey, University of Illinois College of Medicine, 1853 W. Polk Steret, Chicago 12.

Make Plans for—

Wisconsin Academy of Sciences, annual meeting, April 21–22, Beloit College, Beloit, Wisconsin.

South Carolina Academy of Sciences, annual meeting, April 24, Winthrop College, Rock Hill, South Carolina.

National Academy of Sciences, annual meeting, April 24–26, Washington, D. C.

American Association of Petroleum Geologists, Society of Economic Geophysicists, and **Society of Economic Paleontologists and Mineralogists,** annual meeting, April 24–27, Stevens Hotel, Chicago.

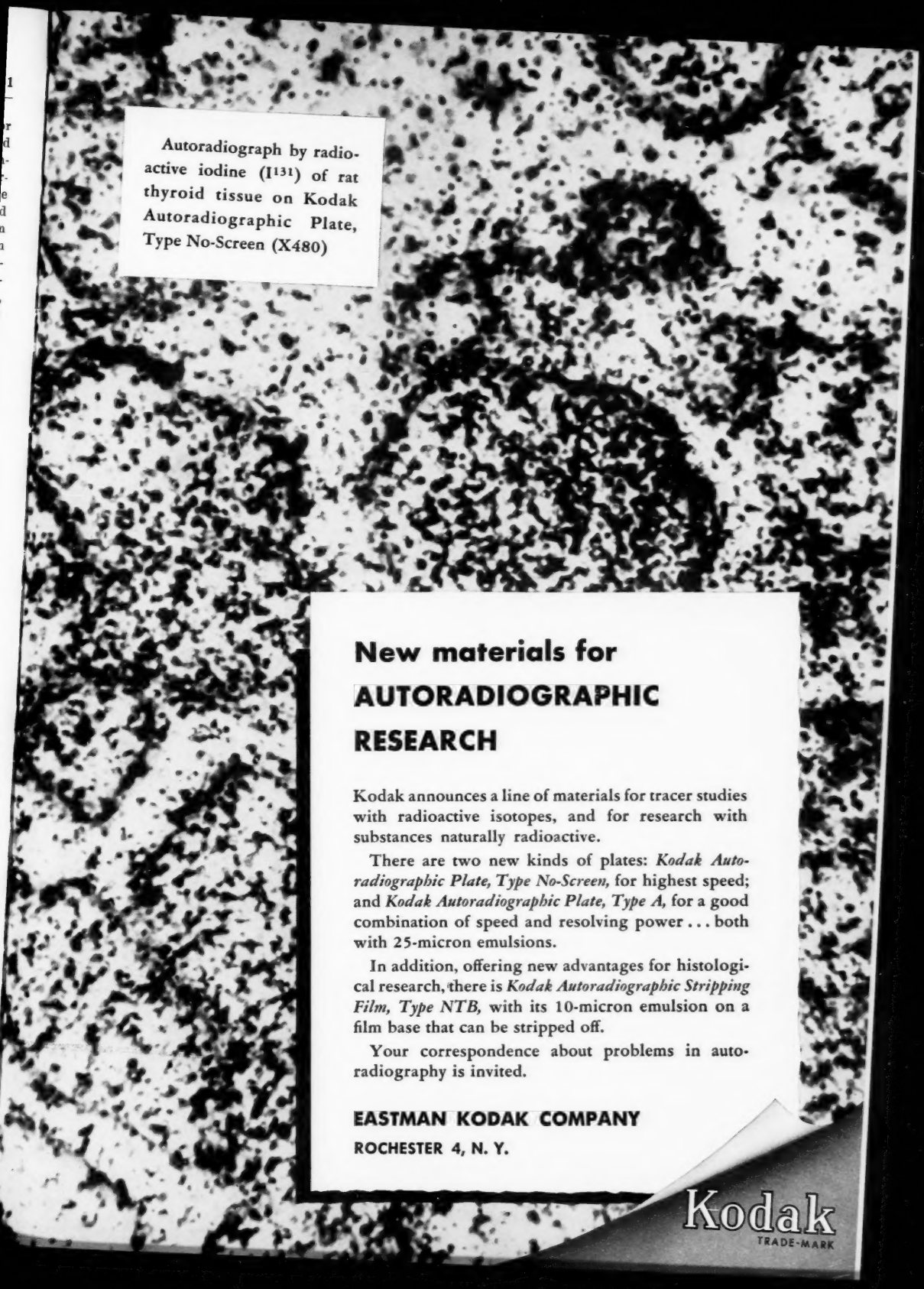
National Tuberculosis Association, 46th annual meeting, April 24–28, Hotel Statler, Washington, D. C.

National Association of Science Writers, annual meeting, April 25, Science Service, Washington, D. C.

American Physical Society, 299th meeting, April 27–29, Washington, D. C.

Ohio Academy of Sciences, annual meeting, April 27–92, Capital University, Columbus, Ohio.

Mississippi Academy of Sciences, annual meeting, April 28–29, Mississippi College, Clinton, Mississippi.



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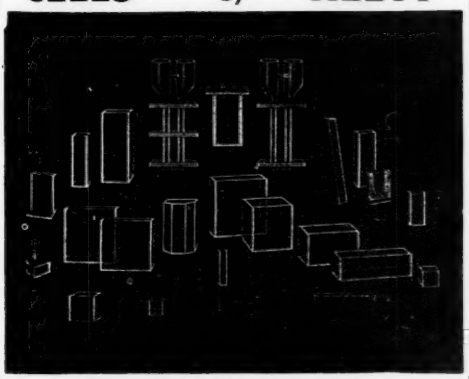

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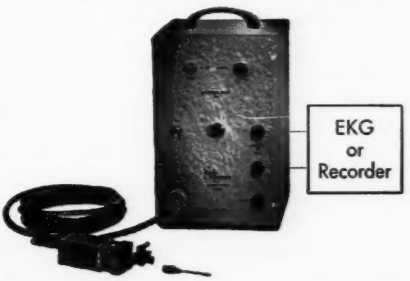

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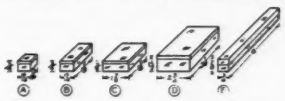

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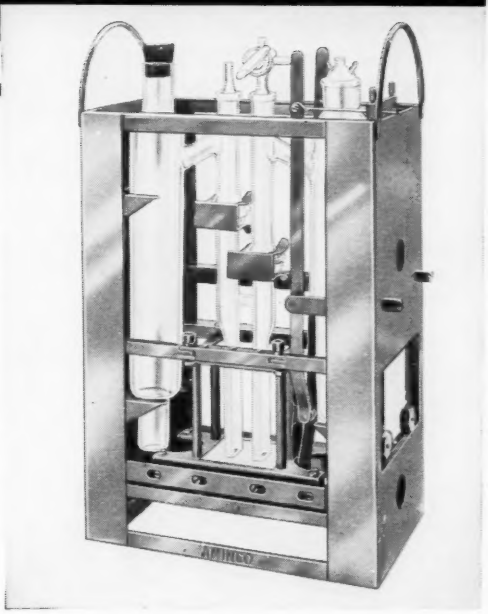

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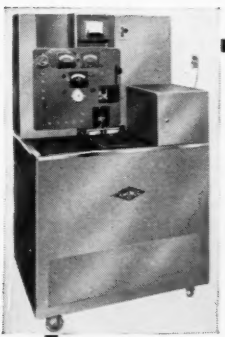

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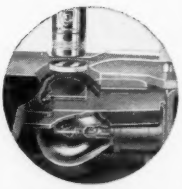

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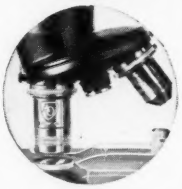

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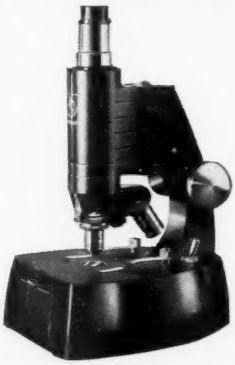

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